Actinomycosis of the Colon, Liver, and Lung. By R. F. C. Leith, M.A., B.Sc., M.B., F.R.C.P.Ed.

Actinomycosis is in many respects a most interesting disease. Clinically, it presents very varied aspects, according to the site of the initial lesion. Beginning usually insidiously and slowly, it steadily progresses, and may have produced very grave pathological lesions before it gives rise to any definite symptoms, and may, indeed, run its entire course, and cause death without affording the physician sufficient evidence of its existence to enable him to give more than a conjectural diagnosis.

Pathologically, it is equally interesting. It has long been classed, like its allies tuberculosis, syphilis, leprosy, etc., as a chronic infective disease, due to the action of a specific organism, named Actinomyces by Harz, a year after its discovery by Bollinger in 1877. Much is known regarding the course and character of the lesions which this organism produces in the tissues, and there are few more beautiful microscopic objects than those presented by the diseased structures when properly demonstrated by suitable staining methods; but many problems still remain somewhat obscure, especially as regards the ætiology, morphology, and exact tissue reactions of the organism. It is sometimes erroneously referred to, especially by veterinary writers, as a new disease, but there is good reason for believing that it was somewhat prevalent among oxen in Scotland some fifty years ago, and the observations of Langenbeck and Lebert, referred to on p. 51, render it probable that it occurred in man quite as long ago. The number of recorded cases has increased greatly in recent years, largely, no doubt, owing to the greater amount of attention which has been paid to bacterial diseases generally. So much is now known regarding the disease that

a correct diagnosis is in many cases possible, and may, indeed, be rendered comparatively easy. This is so where the pus, which in man is such a constant manifestation of its presence, can be obtained for examination. The tissue lesions, produced by it in the organs and structures affected, are so serious, grave, and severe that a correspondingly gloomy prognosis has been necessitated, and where the question of cure or relief could be entertained, the surgeon's knife seemed to be the only remedy. Within the past year or so, however, our hopes have been raised, and it is possible that before long we may be able to regard this disease as readily amenable to treatment.

The cases occurring in this country have been so few that we have not had the same opportunity as our neighbours in Germany and Russia of studying it in its different aspects and phases, and, as the following case presents a more than usually complete picture of these, I need not apologise for giving it in considerable detail. I have much pleasure in expressing my obligations to Dr. Norman M'Kie of Newton-Stewart for his ready and kind assistance in helping me to obtain information about the habits of the patient and early history of the case, and to my colleagues, Dr. Stockman and Mr. Caird, under whose care he was in the Royal Infirmary, for permission to use the case. The nature of the disease was not diagnosed during life.

William D., æt. 23, baker, unmarried; was admitted to the Royal Infirmary, Edinburgh, on 19th September 1893, complaining of pain and swelling in the right side of the abdomen.

The family history is satisfactory and has no bearing on the case.

Personal history.—Previous illness. Patient had measles and scarlet fever when young, and inflammation of the left lung about six years ago. During the latter part of 1892 he suffered a good deal from faceache, and early in May 1893 he complained of not feeling well, and had a cough, some expectoration, and nasal discharge. He was not ill enough to seek medical advice, and soon recovered. He also com-

plained occasionally during the early part of the year of feeling somewhat uneasy and out of sorts, but did not think much about it

Present illness.—On the 15th June he was seized with a severe pain in the abdomen, and a painful swelling appeared in the right iliac fossa and extended upwards and inwards towards the umbilicus. He was feverish and had a short dry cough, but his lungs were apparently quite healthy, as Dr. Norman M'Kie, who saw him at this time, found no abnormal physical signs. In ten days the swelling and pain had disappeared, and he was sufficiently recovered to resume his work early in July. His friends state that his cough and expectoration returned towards the end of August, that he had considerable nasal discharge, which had been present more or less since May, and that he appeared to be losing flesh. He stated himself, however, that he hardly noticed his cough, and that it was so slight that he could scarcely say how long it lasted. He continued well enough to remain at work, but was conscious of a vague feeling of weakness and discomfort in the right side. A distinct pain came on gradually in the right loin behind, and with it a swelling, but he continued to work until the 12th September, when the pain and weakness had become too severe to allow him to do so. Dr. M'Kie saw him again on that day and the next four or five days, and considered his condition to be so unsatisfactory that he advised his removal to Edinburgh. The swelling in the abdomen was larger and higher up than before, the pain continued and became more severe, there was some sickness and vomiting, the temperature kept 1° or 2° above normal, and there were some coarse crepitations towards the bases of the lungs, with cough and some purulent expectoration.

Habits.—Patient was a quiet, reticent young man. He had pretty long hours. His appetite was excellent until lately, when it became poor and capricious. He was very fond of confections, and was very frequently seen to chew them, as well as peas, dry grain, corn, and barley, which he was in the habit of carrying about in his pockets. Large stores of grain were kept on the premises in which he worked.

State on admission—1. *General appearance.*—Patient is fairly muscular and well nourished. He is anæmic-looking. There is no œdema of feet or legs, no jaundice or cyanosis.

2. *Alimentary system.*—Appetite is very poor, but there is no sickness or vomiting. There is much constipation; a motion occurring only about twice a week. This condition has lasted since his illness in June, and it had been present, though not so great, for some considerable time previous to that. There was no pain when the bowels moved, or upon administering an enema. His motions were remarkably scanty even after enemata, but showed nothing otherwise noteworthy. The pain in the right loin is very considerable when he walks, sits, or moves, but is very slight when he lies quietly in bed.

Abdomen.—There is some distension on right side, and its walls are firm and resistant. A mass, somewhat ovoid in shape, can be felt between the lower margin of the ribs and the iliac crest. It passes backwards towards the right kidney, and although it does not reach the middle line anteriorly, there is considerable resistance of the abdominal walls from its inner margin as far as this. It is continuous with the liver dulness in and in front of the anterior axillary line, and reaches to within 1 in. of the anterior iliac crest. It is tender. There is a suggestion of fluctuation when it is grasped between the two hands. Its position and relations to the neighbouring viscera are seen in Fig. 1.

Liver.—Its dulness is continuous with that of mass, but it is apparently otherwise normal.

Spleen is not enlarged.

3. *Respiratory system.*—The cough is very slight indeed. The sputum is very small in quantity, and rather thick and somewhat green. The breath sounds are normal, and there are no accompaniments or other abnormal lung signs. The sputum, examined by the Ziehl-Neelsen method, gave a negative result.

4. *Circulatory system.*—There is nothing abnormal to be noted.

5. *Temperature.*—The morning temperature was 100·°4, the evening 102·°6.

6. *Urinary system.*—Micturition is more frequent than formerly, but is quite free from pain. The urine has a sp. gr. of 1015, acid reaction, many urates, some crystals of uric

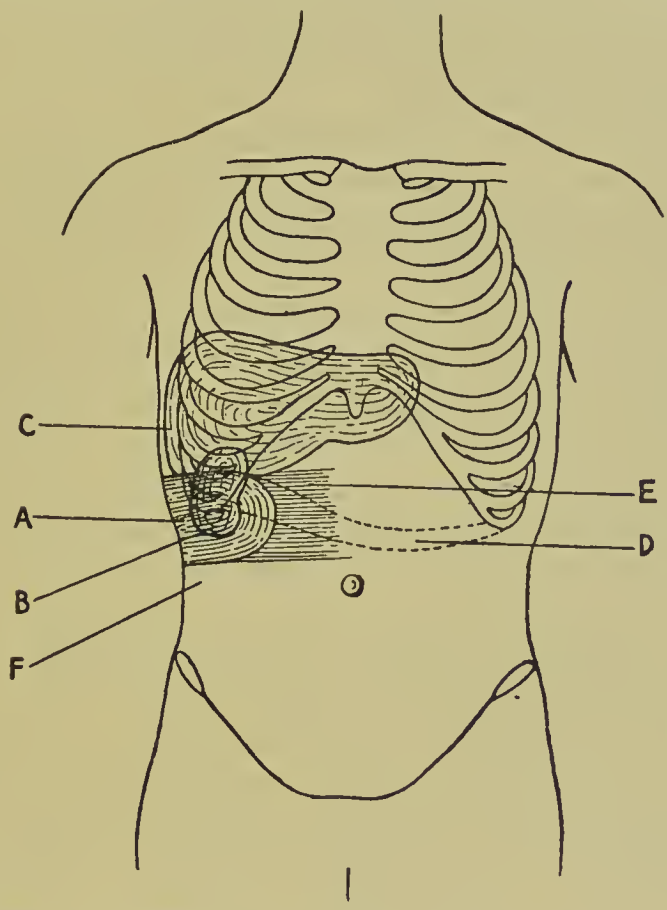

Fig. 1.—This shows the position of the tumour and its relation to the liver, kidney, and colon. The tumour is seen to be incorporated with the kidney and the inferior border of the right lobe of the liver; *a* is the area of absolute dulness represented by the tumour mass; *b* represents the position of the kidney, which was apparently incorporated with the tumour; *c* is the liver seen to be continuous, as shown by both palpation and percussion, with the tumour; *d* is the transverse colon; *e* is the indefinite area to the inner side of the tumour which was imperfectly resistant on palpation; *f* is the area of resonance between the tumour and the iliac crest.

acid, no albumen, no sugar. He passes about 30 to 40 oz. per day.

Diagnosis.—The tumour was apparently in connection with and growing from the right kidney, and was looked upon as probably a sarcoma.

Progress of the case.—The patient remained in much the same condition, his temperature becoming normal in the morning and usually rising in the evening to a little over 101° or 102°, his bowels only moving after an enemata, until the 27th September, when Mr. Caird operated in order to, if possible, remove the tumour.

He first cut down in the lumbar region posteriorly, reaching the kidney comparatively easily. It seemed to be considerably enlarged, but its surface was smooth and presented no palpable lesion, although its upper border could not be reached. He then cut down in front, making a long vertical incision. On inserting his finger he found that the structures were much matted together, and, on exploring the upper part of the wound, he discovered a large tumour, occupying either the lower part of the right lobe of the liver or the upper part of the kidney, and adherent in front to the anterior abdominal wall, he could not determine which, and, as he discovered that the hepatic flexure of the colon was quite gangrenous, tearing at once when touched, he did not consider it justifiable to explore further. He inserted a bent glass drainage-tube, and closed the wound. The patient's pulse remained steady all through the operation, and he rallied well. He passed flatus on the same evening and seemed to be progressing satisfactorily. His condition seemed to improve a little during the next few days, and then his cough began to increase considerably. Expectoration now became fairly copious and crepitations were abundantly heard all over his chest. His temperature, cough, and expectoration led to a suspicion of the development of acute phthisis, but no microscopic examination of the sputum was made. He became steadily worse, and, gradually losing strength, sank and died on the 20th of October.

The post-mortem examination was made by me sixteen hours after death.

External characters.—The body was muscular, and fairly well nourished. There was well-marked lividity posteriorly, and a greenish discoloration of the abdomen. Rigidity was present, and a powerfully offensive odour emanated from the body. There were two surgical incisions on the right side, the one

being anterior in the line of the ascending colon, and reaching from just below the margin of the ribs to near the iliac crest; the other posterior, also vertical, lay over the region of the kidney, and was much more limited in extent. The sutures in the skin and underlying tissues of the anterior incision had given way, disclosing a large, elliptical area of peritonæum, in which the sutures had remained intact. About its centre was a plug of iodoform gauze. On removing this and inserting the finger into the wound, a thickened, matted, and œdematous tissue was felt around the ascending colon. A much softer and more spongy tissue was felt as high up as the finger could reach. A similar exploration of the posterior incision, which passed through all the structures of the body-wall, discovered an œdematous and softened cellular tissue posterior to the kidney, whose posterior surface could be felt to be smooth and firm. Towards its upper border the tissues were much more matted and indurated, and there was a sense of unusual resistance in this region, but nothing definite could be determined. A watery and suspiciously purulent fluid moistened the finger, but no fluid escaped from the wounds. On opening the abdomen, there were obvious signs of an acute general peritonitis. The intestinal coils were moderately distended, and partly glued together by a yellowish lymph. The lymph was present in easily separable flakes and masses, as well as in a diffuse thin covering of the serous surface, which had lost its gloss, and was mostly dull and lustreless. There was also a small amount of fluid pus present. These conditions were most prominent in the pelvis and right side of the abdominal cavity. In the latter position there were evidences of a much older peritonitic mischief, in the form of many fibrous adhesions around the cæcum and ascending colon. These structures were firmly bound to the posterior abdominal wall—the cæcum being almost embedded in the right iliac fossa. The tissues around it and the ascending colon, besides showing a thickened and matted condition from a previous peritonitis, exhibited much purulent and œdematous infiltration of a recent character. The vermiform appendix required a somewhat careful dissection before its position and relations were seen. Its place of origin from the inner border of the

cæcum was comparatively easily detected by tracing downwards the anterior longitudinal muscular fasciculus in the wall of the ascending colon and cæcum. This simple plan cannot be too strongly recommended. In the course of an investigation upon the cæcum and vermiform appendix, in which I have examined over 400 cases, I have very rarely found it fail. In ordinary cases, where anterior adhesions are not present, it leads clearly and unmistakably, being very easily seen, to the origin of the vermiform, spreading a little just as it reaches it. In cases where extensive adhesions or other changes have occurred in this region, it is extremely rarely so obscured as not to be available, so that the surgeon will find it an unfailing guide. In the present case the bulbous origin of the appendix alone was visible, and nothing could be seen of its further extent and direction. It was afterwards found to run upwards, with a slight inclination inwards, behind the ileum and along the inner border of the ascending colon posteriorly, being entirely surrounded by much thickened œdematous and purulent cellular tissue. This had apparently originated in the parts around the appendix, and not spread from it, as its peritoneal coat was but little altered, while its other coats and its lumen presented no unusual feature.

Hepatic flexure of colon.—In the region of the hepatic flexure of the colon there was much soft, spongy-looking material of a brownish yellow colour and foul odour. On attempting to handle it, brownish liquid fæces escaped into the peritoneal cavity, which had been noted previously to be free from all sign of fæcal invasion. Nearly the whole extent of the hepatic flexure was in this condition; no definite wall being discoverable. The upper border, next the liver, was firmly adherent to the under surface of that organ, and presented the appearance of a yellowish-black sloughy-looking layer, while the rest of it was represented by the friable gangrenous substance already referred to. This was also seen to have been adherent to the parietal peritonæum of the anterior abdominal wall. It gradually passed into the more resistant wall of the gut, which showed for some distance along its peritoneal surface a blackish pigmentation of

irregular distribution. The rest of the large intestine appeared to be healthy. There was no obvious obstruction in any part of the large gut, so that the passage for fæces was free. These were present in fair quantity, in a somewhat liquid condition, and of a yellowish-brown colour, throughout its whole length. The mucous membrane was quite healthy, except towards the hepatic flexure, where in both the ascending and transverse parts it was a little softened, paler, and discoloured. The softening and thickening soon spread to the whole wall as the gangrenous area was reached. No whitish patches or foci were seen. The small intestine was perfectly healthy throughout. The duodenum, as it lay in such close proximity to the liver and hepatic flexure, was most carefully examined, but showed no sign of any abrasion or cicatrisation of its mucous membrane or other change in its wall. The stomach contained a small quantity of light brown granular fluid and small masses of cheesy substance. Its mucous membrane and wall were healthy.

The liver.—The lower margin lay 1½ to 2 in. below the ribs. The upper surface showed some recent lymph, on the right side, and a few old inflammatory adhesions, uniting it to the under surface of the diaphragm. It was of a markedly yellow colour, except near the anterior border of the right lobe, where it was greenish black. On raising this border, the part of the under surface adherent to the colon came into view, and presented a peculiar appearance. It was of a deep black colour, showing small, closely-grouped, white nodules, which, on being pricked, were seen to be abscesses. The outer surface of the right lobe of the organ was firmly adherent to the abdominal wall for an area of ¾ in. in length, and rather less in breadth. On cutting it away a number of minute abscesses with pigmented walls were cut across. The appearance thus closely resembled that seen on its under surface, but the pigmentation was not so extreme. The abdominal wall was implicated in part of its thickness only, the peritoneal and most internal muscular layers alone being infiltrated. There was a considerable amount of old inflammatory tissue on the under surface of the right lobe, where it came in contact with the suprarenal capsule and surrounding

tissue; but otherwise this part of the surface of the organ presented nothing observable. The liver, with its adherent

Fig. 2.—Is a photograph of a section through the affected part of the right lobe, slightly reduced in size. The preparation is now in my museum. The honeycomb-like network of abscesses is very well seen. The abscess cavities are seen to vary somewhat in size, but are mostly small.

piece of colon, was then removed. It weighed 4 lbs. 14 oz. It was very flabby and friable, and generally of a yellow colour. There was nothing abnormal, as seen with the naked

eye, exeept the appearanees at the two plaees already mentioned, but a resistant tumour-like mass was felt occupying part of the right lobe, and apparently eoming to the surface at these two places. A transverse section was made through the organ, so as to pass through the long axis of the tumour mass in the line of its greatest transverse extent. This line was somewhat lower than the area of adhesion to the body wall. It disclosed a remarkable condition, whieh is represented in Fig. 2.

The mass was seen to oceupy the under part of the right lobe towards the right side, and measured $4\frac{1}{4}$ in. in its greatest transverse, and 4 in. in its greatest vertical extent, while it varied from $\frac{1}{2}$ to 2 in thickness. It showed a fine reticulated strueture, the meshes of whieh were filled with pus, which welled forth from every part of it. These abscess cavities varied considerably in size from the minutest points to that of a bean or even larger. They had outlines of many shapes, some, espeeially the minute ones, nicely rounded, others oval, others irregular. The walls were of varying thickness, from that of a mere shell often apparently quite smooth to $\frac{1}{16}$ in. or thereabouts, and more deeply pigmented, being blaek or slate-coloured. Their contents were fluid, white, and slightly slimy, having all the ordinary characters of pus. While it was mostly white, it was here and there tinged a varying shade of yellow, and there was no observable difference between the pus of the central and peripheral cavities. A number of little whitish bodies were seen lying in the pus, and in order to get a good view of these a wide mouthed glass tube was taken, and, some of the pus having been plaeed in it, was inelined and rotated so as to spread the pus in a thin layer all over the inner surface. The minute bodies were then clearly visible, being seen adhering to the tube in immense numbers. They varied in size from a pin-point to an ordinary sized pin-head. The smallest were transparent and translucent, looking like little specks of colourless jelly; while the largest were opaque, white, palc yellow, greyish, or even greenish in colour. Many of them, which were of a distinctly saffron-yellow colour, when seen by reflected light, were of a greenish hue by trans-

mitted light. They were obviously actinomyces colonies, and the case one of actinomycosis. The margin of the actinomycotic mass was sharply defined from the liver substance; it

FIG. 3.—Is a photograph of a section near the margin of the mass, slightly reduced in size. The older part of the growth is seen to the right, while the encroaching margin is seen to form somewhat lobulated out-growths, in which the reticulated nature of the tissue is well seen.

was for the most part fairly well rounded as if encapsuled, with, however, many pigmented, fibrous bands radiating outwards into the liver for a short distance from the capsule. Towards the deeper parts of the growth this appearance was

lost, the outline becoming very irregular, showing rounded, lobulated, and finger-like invasions of the liver substance, as seen in Fig. 3.

In these the minute abscesses, with their delicate, pigmented walls, were well seen. The rest of the liver was advancedly fatty; but in no part were abscesses seen distant from the main mass, all the prolongations being seen to be in direct continuity with the main growth. This is not always so, as was exemplified by a case which has been carefully described by my colleagues, Grainger Stewart and Muir in Vol. I. of these *Reports*, at the post-mortem examination of which I was present, and part of the liver of which is now preserved in my museum. It shows several small abscesses a short distance away from the main mass, which was moreover much larger and more irregular in shape than that of the present case. This appearance is also described by Dr. Taylor[1] in another case in which several little white grains, like miliary tubercles were seen, both on the surface and on section, at a distance from the main honeycomb-like mass. Mr. Shattock[2] and others have made similar observations; but, while this reticular or honeycomb-like arrangement of abscesses is undoubtedly the usual appearance which an actinomycotic growth in the liver shows, other observers, *e.g.* Mr. Eve,[3] have described a different form in which definite cheesy nodules were seen, without the formation of abscesses. I may also note that, both in Dr. Taylor's case and mine, the actinomycosis had spread to the lateral wall of the body on the right side, and, had the patient lived, would have led to the formation of an abscess in the midaxillary line about the seventh or eighth ribs, which might have been the first indication inducing him to seek medical advice. A glance at the recorded cases of abdominal and other forms of actinomycosis will show how frequently this abscess pointing is one of the first prominent indications of the disease; abscesses having been observed and opened in almost every region of the parietes in the abdominal region, in the thorax and neck.

[1] *Guy's Hospital Reports*, 1891, vol. xlviii.
[2] *Trans. Path. Soc. London*, 1885.
[3] *Ibid.* 1889.

A few of the actinomyces bodies of different sizes were selected and examined microscopically. They were first mounted, unstained, in Farrant's solution. The very small ones were difficult to differentiate, presenting the appearance of bright, somewhat ill-defined, radiating filaments. Larger ones were of a spherical shape, with an opaque, granular centre, with masses of yellow, brown, and black pigment irregularly distributed in it, and a peripheral appearance of threads. These threads became more evident after using acetic acid or a dilute solution of caustic potash. On staining with eosin the peripheries of the spheres became more evident, showing in places a structure suggestive, but by no means distinctive, of clubs.

A number of cover-glass preparations were then made from carefully selected parts of the pus, so as to represent as nearly as possible an ascending series as to age of the actinomyces bodies. These were stained by Gram's method, and examined with a Zeiss $\frac{1}{12}$ oil immersion, and Oc. 4.

The smallest colonies are found to be so small as to be quite invisible to the naked eye. They present many varieties in shape, some being nearly star-shaped, with filaments radiating outwards from a common centre, which also varies considerably in size and density, others forming a dense, short, oblong, or irregular mass, with filaments radiating regularly or irregularly from it on every side, others forming loose networks, or little, entangled networks, and so on. The filaments in all cases closely resemble one another. They are always delicate and thread-like, of fairly uniform thickness throughout, though often ending in slight bulbous extremities. A few are slightly coarser than the others, but the difference is always slight. The average breadth is about ·4 to ·5 μ. They are mostly wavy and sinuous, some showing perfect spirals, others bending and twisting, interweaving and intertwining in all directions. Occasionally a little isolated cluster will show one filament coiling like a twining plant around another, with one or two other filaments or bits of filaments hanging on. A few filaments are nearly straight. Branching is frequent, though it is often merely simulated by an accidental arrangement of the

filaments. It is more frequently lateral than dichotomous, and when the latter the branches rarely seem to be equal. A few rounded forms, like cocci, are seen among the filaments. The larger actinomyces bodies are made up of similar colonies, growing in various directions, and more or less complexly grouped together with a various admixture of golden yellow pigment. Appearances were here and there seen suggestive of clubs, but I could not satisfy myself about them. In some parts of the older colonies nothing but pigment in little club-shaped pieces and broken interweaving threads could be detected, suggesting a transformation both of filaments and clubs into pigment. I ought to remark that considerable care had to be exercised in flattening out the larger colonies, as they were too dense to allow of microscopic examination in their unaltered shape. It is somewhat surprising that very few of the filaments, even in the youngest colonies, showed a continuous homogeneous protoplasm. Their contents were mostly broken up, sometimes by few, sometimes by many gaps, so as to give the appearance of long or short rods or cocci, closely or sparsely scattered along the course of the filaments.

In most cases these forms stained deeply as if they were spores, in others poorly, as if they were the degenerated remains of the protoplasmic contents of the filaments.

Besides the pigment present in the actinomyces bodies there was an abundant black and slate-coloured pigmentation, irregularly distributed throughout the peritoneum and in the walls of the abscesses in the actinomycotic mass. It was unaltered by washing in water, but gradually disappeared under the prolonged action of alcohol. I have seen a similar blackish pigmentation of the peritoneum under many conditions, notably in pyæmias. In one of these the liver was the seat of several abscesses closely grouped together, the pus from which showed a number of variously-sized bodies closely resembling, to the naked eye, the actinomyces colonies, but, on microscopic examination, found to be shreds of tissue; the only organisms present being many micrococci and the *Streptococcus pyogenes*. In this case, however, the pigmentation had not spread to the walls of the abscesses. It is said that

this black pigmentation, seen in abdominal actinomyces, is due to the formation of sulphide of iron, probably as a post-mortem change caused by a reaction between sulphuretted hydrogen escaping from the bowel, and the pigment proper to the actinomyces. This pigment is not soluble in water or alcohol, but partially so in ether or chloroform, and is elaborated by the actinomyces. Its presence in the colonies must have an important influence upon their naked-eye characters, which, so far as I could determine in this case, depended chiefly upon the amount of pigment present and the complexity of the colonies arising from their growing together in groups. Klebs, Boström, and others, hold that the presence of clubs has also an important influence. They say that the younger actively-growing colonies, having no clubs, are almost transparent, while the older slowly growing ones, having clubs in abundance, are white or yellow. We shall presently see that, in this case, clubs are present in great numbers, although I was so far unsuccessful in seeing them, and thus may have materially contributed to the variations in the naked-eye characters of the bodies. I have looked at these bodies from time to time, as they still adhere to the inner side of the glass tube, and noted that, while the smaller ones gradually disappeared, many, especially of the larger ones, continued to be perfectly recognisable. This is the case still, at a period of over two months from the time of their collection. Besides the actinomyces colonies, the pus contained many other organisms, notably micrococci, streptococci, and various bacilli, exactly similar to those seen in the pus taken from the abdominal cavity, with, in addition however, many thin bacillary forms, straight, wavy, curved, twisted, etc., which are most probably separate young filaments of actinomyces. Cover-glass preparations were also made of the pus found in the peritoneal cavity on first opening the abdomen. With the naked eye no bodies were seen, and under the microscope no undeniable colonies or filaments of actinomyces could be detected. It was, however, rich in organisms, the following forms being all that were seen after careful searching:—

(1) Many separate micrococci. (2) More commonly arranged as diplococci. (3) Often also as short chains of three,

four, or five, rarely more, elements, often unequal in size. (4) There is also another diplococcus twice the size of (2), often occurring in pairs or even two pairs in a line, so as to resemble a chain. Among the bacillary forms (5) the commonest was a short form, occurring like the diplococcus in pairs, their contiguous faces flat, and their distant ends rounded. They frequently presented a capsule-like appearance, but I failed by Löffler's and other methods to bring one out. (6) Another form not unlike the last, but more like Fränkels pneumococcus, was also sparsely present. (7) Another most remarkable form was sparingly present. It is about three times as thick as the tubercle bacillus, of greatly varying length, 2 to 10 μ, with rounded ends, often quite straight, sometimes slightly curved, or even wavy, occurring singly or in whole chains of a few unequal elements. This form was also noticed by Muir in his case. (8) There was still another form about half as thick as the last, about 5 to 6 μ long, with rounded ends. (9) A thin, short, straight form about as thick as the actinomyces filaments, with rounded ends, was the least frequent of all, many microscopic fields having to be searched before finding one

The spleen.—It weighed 14 oz., was soft and pulpy, and of a pale red colour. There were no signs of any suppurating points or other lesion.

The kidneys.—The right kidney weighed 9 oz. There was much chronic inflammatory change around it; its upper border with the suprarenal body being firmly adherent to the under surface of the liver. On its anterior surface, close to the entrance of the renal artery, there was an appearance of a number of points, pale or reddish, closely grouped together, and others more scattered. I regarded them at the time as possibly actinomycotic foci, which had arisen by direct extension from the diseased colon, under which this part of the kidney lay. They were not confined to the capsule, which was somewhat adherent over them, though not elsewhere, but invaded the cortex for short and unequal distances only. On pricking them with a sharp-pointed knife, no pus exuded. Further, there were no visible abscesses between them and the overlying diseased colon; and the possibility of

there being non-actinomycotic, and of independent origin, clearly presented itself. The superficial cortex was somewhat swollen and paler than normal, which was probably due to a cloudy-swelling plus, the result of decomposition. The left kidney weighed 8 oz. and closely resembled its fellow, but showed no implication of its capsule.

The suprarenal bodies.—Both were healthy.

The pancreas.—It was moderately firm, pale, and showed no lesion.

The mesenteric glands.—A few were swollen, and one near the pelvis was the seat of a small abscess, the pus from which showed micrococci, the *Streptococcus pyogenes*, and apparently no bacillary forms. The other mesenteric and all the vertebral glands were apparently unaltered.

The vertebræ.—They were quite unaffected.

None of the abdominal organs gave any waxy reaction with iodine.

Thorax—The heart.—The pericardial cavity contained $4\frac{3}{4}$ oz. of clear fluid. The arterial and cusped valves were healthy. The cone diameters were, pulmonary 1·05, aortic 1·0, tricuspid 1·4, mitral 1·35. The cardiac muscle was pale, flabby, and friable, and was the seat of a diffuse and somewhat extensive fatty change, but showed no other lesion. The pericardium was healthy. The heart weighed $13\frac{1}{2}$ oz.

The lungs.—The right pleural cavity contained about 9 oz. of clear fluid, which showed no distinctive macroscopic or microscopic characters. There were no adhesions. The right lung weighed 2 lbs. 1 oz. Its pleural surface was smooth and glistening, except on its diaphragmatic aspect, which showed a delicate layer of recent lymph; an early acute pleurisy, which had obviously spread through the diaphragm from the peritoneum. On section, the lung substance was seen to be venously congested and œdematous, especially in the lower lobe. At first sight this seemed to be all that was wrong, but a careful examination discovered quite a number of tiny areas of pus. The largest of these were about twice the size of a pin-head, and seemed mostly to correspond to minute bronchi. The smallest ones only became visible by

the specks of pus which exuded on squeezing the lung substance. A fairly large amount of pus could thus be expressed from most of the medium and small bronchi. I could not, with the naked eye, determine whether these cavities also were minute bronchi or of new formation. The larger suppurative areas were present in small numbers in the upper lobe, and rather more plentifully in the middle and lower lobes, especially towards the base. The larger bronchi are a little congested and contain some muco-purulent fluid. The left pleural cavity also contained nearly 9 oz. of clear fluid. There were no adhesions. The left lung weighed 1 lb. 12 oz. and showed obvious evidences of diaphragmatic pleurisy, which were, however, less marked than upon the right side. On section, it closely resembled its fellow, but its suppurative points were much fewer in number. No other lesion was present in either lung, as was proved by dividing the substance in every direction into small pieces. There were no miliary or broncho-pneumonic or other nodules, no cavities, induration, or other lesion, such as is generally met with in pulmonary actinomycosis. Only a small quantity of the pus was collected and spread out into a thin layer, but, with the naked eye, no actinomyces bodies could be detected in it. On microscopic examination, however, they were clearly demonstrated, though comparatively small numbers of typical colonies happened to be present. Abundant clusters of micrococci were present, often forming dense masses, at the periphery of which, as well as at a distance from them, were finely formed streptococci, in many of which it could be seen that the round deeply-stained cocci really lay in a colourless filament, resembling a fine capillary tube. I had little doubt from their appearances that these also represented actinomyces filaments. The other organisms already described as being present in the abdominal pus were also observed here, especially the large bacillary form (7), which was present in great numbers. This enumeration, however, does not include all the forms, as other bacilli, differing somewhat in minor detail, were also observed, notably a short bacillus occurring in pairs, one of which was generally of the clostridium shape. There were, moreover, many of the fine bacilli

straight and curved, which have been already mentioned as occurring widely spread throughout the pus in the liver, and which I am inclined to look upon as young stages of the actinomyces filaments. The bronchial glands, vertebræ of thorax and neck, thyroid body, and other structures of the neck were all carefully examined, and showed no change. The jaws and structures in the mouth were unaffected, and the teeth were apparently in good condition, except a broken incisor. There was a slight discoloured appearance and some tartar at the root of one or two; but scrapings of these showed no trace of the actinomyces when examined microscopically.

The brain.—Weighed 3 lbs. 8 oz., and both it and its membranes were apparently quite healthy.

In order to obtain a more complete examination of the case, pieces of all the organs were placed in saturated solution of corrosive sublimate and some in absolute alcohol. They were subsequently embedded in paraffin and cut with a rocking microtome. Various methods of staining were employed—(1) Gram's method: eosin, orange, Bismarck brown, Biondi, safranin, and picro-carmine being all used as contrast stains; (2) Ehrlich's new histological stain (logwood and orange rubin), both alone and in combination with Gram; (3) Carbol-fuchsine and Gram; (4) Carbol-fuchsine and methyl-blue. The best results were obtained by Gram's method. This seems to be the universal experience of observers. It was first used in England by Acland. It brings out the filaments and cocci extremely well, while the clubs can be brought out at the same time by using a strong solution of eosin as a contrast stain. I found that a fairly strong solution of orange rubin answered this purpose still better, and I succeeded in demonstrating them better with it than with either eosin or carbol-fuchsine. Another method, that of Weigert, has also been used to demonstrate the clubs (viz., Wedl's solution of orseille, using gentian-violet as a counter-stain). The clubs here stain a deep red colour. There are other special methods favoured by other observers. A good account of different methods is given by Delépine.[1]

[1] *Trans. Path. Soc. London*, 1889, pp. 131-136.

The liver.—The pieces of the liver were taken from the under surface, including the adherent colon, the margin of the growth to either side of this, both right and left margins, and that representing the deepest and most active part of the growth furthest away from the colon. Further, the complete contents of some seven or eight abscess cavities of various sizes and from different parts were scooped out and allowed to fall into a saturated solution of corrosive sublimate. These coagulated masses were treated in the same way as the sections, embedded in paraffin, and cut with the rocking microtome. Serial sections of these as well as of the liver sections were carefully studied, so as to obtain a correct appreciation of the different appearances presented by successive sections of the same actinomyces bodies at different levels; for, being spherical, very delusive conclusions might otherwise be drawn regarding the appearances at different ages.

Under a low power the actinomycotic growth is seen to invade the liver substance and to show multiple abscesses spreading by continuity. These are more or less completely filled with pus, in which the actinomyces generally lies. It will be convenient to describe first the colonies and then the lesions which are found to accompany them.

The actinomyces.—While the organism is easily seen with the aid of ordinary low powers of 50 diameters, and ordinary high ones of 250 or 300 diameters, the appearances, herein detailed, were always verified by the use of Zeiss $\frac{1}{12}$ oil-immersion lens and a No. 4 eye-piece. It would be both tedious and profitless to describe the many different appearances presented by the colonies, as these can all be probably correctly regarded as related by peculiarities in growth or line of section to three or four main growth forms. These are—

1. *The radiate colony*, like a many-armed starfish, or the burr-like heads seen on some of the common climbing plants of our hedges. (This is represented in Plate I. Fig. 4, *c*.) The central part is composed of densely interwoven filaments, with cocci lying in a basis of granular hyaline material, which stains red with eosin. It varies greatly in size and density in different colonies. In some it is quite easy to see the separate filaments, in others it is so dense that it is impossible

to completely resolve it. Even then, however, filaments, numerous cocci, and bacilli can be made out, especially at the margin of the dense parts. The cocci forms appear to be more numerous the denser the areas are. From these dense areas the fine thread-like filaments radiate outwards in every direction, so that for the outer two-thirds of the radius of the sphere-like mass, the constitution of the colony can always be clearly seen. These filaments have already been described, but it is now noted that far more frequently than before they present a homogeneous, unbroken, deeply-stained protoplasm. The minute bulbous ends of some of the filaments are well seen. The straight filaments especially show them; they stain as deeply as the rest of the protoplasm of the filament, and are not in any way differentiated from it. The bulbous end is occasionally seen to curve round after the fashion of a walking-stick. The hyaline or granular red material occupies the intervals between the filaments, and sometimes beyond their ends, except here and there where the pus corpuscles have invaded it, and lie between the ends of the filaments. A comparatively small number of cocci forms are seen to lie in this matrix of the peripheral part of the colony. They might be regarded as the ends of filaments cut transversely; and, from their size, number, and distribution, I am inclined to regard this as the correct explanation of most of these peripheral cocci forms. A few short filaments, probably pieces broken off from long peripheral ones, are often seen lying in the pus some little distance away from the margin of a colony; in fact, it is not uncommon to see long filaments coming out here and there from the periphery of the colony, and advancing into the pus far beyond the others. Pus corpuscles may be seen which have ingested fragments of filaments. Clubs may be entirely absent from these colonies or present in considerable numbers. They occupy the periphery of the colony, generally extending a little distance beyond the ends of the filaments. They often appear in slightly thicker sections to lie tier upon tier, the lower always being a little further out than the one above it. They are nearly all of a slender club shape, though a few are pear-shaped. They show a homogeneous structure, and, while the

majority are fairly alike in length, a few scattered ones pass, like the filaments, far out from the periphery into the pus.

2. *The oblong or arc colony.*—This shows an extension of the dense central portions of a colony in one plane, so as to form an oblong or curved, solid, cylindrical mass from the periphery of which filaments radiate outwards in every direction. (This is seen in Plate I. Fig. 4, *f*, *l*, and *q*.) This central part shows a deeply-stained mass, far too dense in the majority of them, even in the thinnest sections I could procure, to allow its structure to be made out (*vide* Fig. 4); but an accidental longitudinal division of one or two of them, nearly in the centre, allowed a better view to be obtained. Very numerous cocci and short bacilli were thus seen, closely resembling the appearances seen at the immediate periphery of the dense part, where it begins to open out a little, thus making it almost certain that it contained only immense numbers of cocci and bacilli, with probably some filaments. A few of them are sufficiently open to disclose a dense network of filament, as in Figs. 7 and 8, Plate IV. Around the periphery of many of these colonies clubs are are seen in immense numbers. They are mostly slender clavate forms, such as are described above, but some larger, branched, fan-shaped, or palmate forms are occasionally present, standing out like buttresses from the margin of the colony, causing it to have an irregular outline. The central part of the colony often shows a granular or typical mosaic pattern, resulting from the transverse sections of clubs. Small and separate clusters of clubs like banana bunches or rosettes, with few or no filaments, are not infrequently seen quite close to the colony, or scattered irregularly through the pus. These may also be sometimes noticed in the vicinity of the younger radiate colonies. Sometimes only one side of the colony shows a continuous margin of clubs, the other showing none or only a few in little patches. Again, the patchy appearance may prevail all round. There may appear to be many circles of them, or only one around the periphery, and the larger forms of buttress-like arrangement are fairly common. Broken ends of clubs are also seen lying near the periphery.

3. *The round or hollow sphere colony.*—This shows an

extension of the dense portions, so that the curved cylinder meets all round, forming a hollow sphere. The contour is often deficient, but perfect spheres are not infrequently seen. (This is seen in Plate I. Fig. 4, *j*.) Filaments radiate more plentifully from the convexity than from the concavity, so that the centre is hollow, but occasionally those from the concavity are so many and so long that they, more or less, completely fill the space. In one or two instances the hollow of the sphere is seen to contain leucocytes variously degenerated. The spheres sometimes do not preserve a convex outline throughout their growth, but become flattened in one or more places. This irregularity of contour is still further increased when, as sometimes happens, thick shrub-like outgrowths project outwards from the periphery, and give off filaments like the rest of the growth. (This is shown in Plate IV. Fig. 8.) The characters of the filaments and cocci and the ground substance are mostly similar to those of the other forms. Clubs are very frequently present, sometimes both on the outside and the inside, but more usually only, or best seen, on the outside. They present much the same varieties and characters as those seen in the last arrangement.

4. *The loose reticular colony.*—While many of these are undoubtedly merely the separated peripheral parts of other colonies, there are others apparently representing independent colonies. The filaments retain a loose arrangement throughout, and while one part may be denser than the other, all parts are really open. They form masses of irregular shape, but also show a tendency to grow round, so as to form hollow spheres. Cocci forms are sparsely present. There is generally much granular or homogeneous ground substance, and slender clubs are often seen. It is quite possible that this form may be a modification of the first. Such a colony is seen in Plate I. Fig 4, *h*.

When it is considered that these growth forms may be cut in many different ways, and further that they may originally, or in the course of their growth, come to lie in close proximity to one another, it will readily be understood how varied and different will be the appearances they present.

It is only after a careful study and comparison of many serial sections that we are able to simplify the appearances, and reduce them all to different manifestations of a few growth forms.

The first and probably the fourth are young, quickly-growing colonies, which, finding their habitat and surroundings suitable, are able to develop unhindered. The second form is of slower growth, probably because it soon meets with conditions more or less unfavourable to its free and spontaneous development. The third form may be looked upon as closely related to the second, which, it will be remembered, was described as oblong or curved like a bow, according as the dense growth took place in a straight or curved line. As it cannot grow on continuously in a straight line, it sooner or later begins to curve round in the form of an arc of a circle. By a continuation of growth in the same direction the two ends may approximate and complete the circle, thus giving rise to the hollow sphere form. Boström [1] in his most able and exhaustive paper, traces in most careful detail the growth and development of the young colonies until they reach maturity. He lays great stress upon the manner in which the colonies are built up until the mature or hollow sphere form is reached, and this he regards as the typical colony. His description of the forms corresponds to a certain extent with that given above. He recognises a young, an oblong, and a hollow sphere form, and considers that the first grows out into the second, and then bends round so as to form the third. It is difficult to determine whether this bending round is the result of physical or vital conditions. It can hardly be held to be due to conditions of environment alone, as then, in all probability, there would be many more irregular forms. It is much more likely that it is an inherent character of the colonies, after a certain time, to adopt a curved growth just as true twining plants do; and that the rapidity of growth of the constituents of the colonies is greater upon the convexity than upon the concavity of the arc. Indeed, in one of the hollow sphere forms seen in one of my sections, an appearance is presented not unlike the

[1] "Untersuchungen ueber die Aktinomykose des Menschen," *Ziegler's Beiträge zur Path. Anat.* 1890.

section of the simple ovary of a plant showing sutural placentation, for not only have the two ends grown round so as to meet, but even after that one of them has continued to curl and presents its curved end within the sphere. A somewhat similar condition is represented in Plate IV. Fig. 8, where the dense parts, after meeting, have grown outwards again, and in it the dense growing part is more open than is usually the case. This could not take place in such a dense felted tissue as the parts of these hollow spheres exhibit, except as the result of a special manifestation of growth. It is extremely tough, tenacious, and resistant, so that a bending is in the highest degree improbable. I am unable, therefore, to follow Boström's description of the manner of formation of these hollow sphere forms. Muir[1] also says that he was unable to trace this mode of formation in his case. Boström further only figures and describes clubs as buried in the substance and radiating from the outside of the dense part of the sphere, while a few of my specimens show them also upon the concave part. It is somewhat remarkable that as these clubs, which have now been seen to be plentifully present in many of the colonies of all ages, were not observed by me in examining the fresh specimens and cover-glass preparations of the pus. Many observers have seen them much better in fresh specimens than in stained ones, so that my experience in this case would appear to be somewhat exceptional. It may be that the clubs are here present in relatively small numbers, compared with their cases, being apparently absent in many of the colonies, and that I happened to select some of these for examination. Further, there is a great tendency for the young clubs, at anyrate, to get dissolved and washed away in the pus and other liquids. It will be necessary before leaving the consideration of the morphology of the colonies to discuss the relationship which the various elements of the colonies, the filaments, clubs, and cocci bear to one another, but I shall defer this question till I have noticed the presence and characters of the colonies themselves in the intestinal walls and lungs. I shall, therefore, now pass on to consider the lesions in the liver. These have already been described to a certain

[1] *Edinburgh Hospital Reports*, vol. i. p. 107.

extent, but it is necessary to consider them more in detail, viz., the abscesses, their contents, walls, and surrounding structures, etc. Microscopically the abscesses are seen to vary in size and shape, and some to open by channels into one another. They are filled with pus which usually shows one or more actinomyces colonies. These most frequently lie, like little islands, surrounded entirely by the pus, but they not uncommonly lie close to the wall of the abscess, with a very thin layer of pus, or none at all, between them and the wall. The pus almost invariably comes right up to the margin of the colony, and is usually seen to invade its periphery in places. This is extremely well seen where the outlying margin of a large mature colony is seen in the section, when the filaments occur in little masses separated by clusters of leucocytes, thus presenting the appearance of a colony successfully invaded in many quarters and broken up into isolated areas by the victorious leucocytes. Such actual invasion may take place; for a study of serial sections showed that some of these cases could not be referred to such outlying parts of large colonies, as they, in fact, themselves represented the main part of their colony growths. Such a condition probably indicates an inhibition and retardation of growth leading to a successful invasion and disruption by the surrounding leucocytes. Comparatively few colonies are seen where the pus does not come quite up to the margin. The pus is seen to consist of cells, varying somewhat in shape, size, and character. Most have an irregular shape, while a few are definitely rounded. Their protoplasm stains fairly well, or very feebly, and is mostly much degenerated, showing fatty and other globules. The nucleus also varies, sometimes single, sometimes double, often lobed, and showing great variety in the amount of chromatin substance present—many apparently having none, while many stain very deeply. The great majority of the pus cells are obviously degenerated leucocytes, but some are altered connective-tissue cells. The latter are far more numerous towards the margins of the abscess cavity, and also at certain places in these cavities, where there are traces of formerly distinct cavities. There is a considerable amount of granular débris, often seen among the

cells, arising mostly from broken-down leucocytes, but also to a certain extent from red blood corpuscles. Very few recent red blood corpuscles are to be seen. Larger granular masses are occasionally present, which may have arisen in this way or from degenerated giant cells, or even small colonies.

Among the pus cells, sometimes even in them, are a few cocci, bacilli, and short, single threads, or small clusters of actinomyces. These are seen everywhere in the pus, though especially abundant near a colony, and have been already referred to as probably broken ends of some of the filaments of the colony. Obviously, however, some of them may be the nuclei of growths of young colonies. In addition, there are sometimes the small clusters of clubs to which reference has already been made. The wall of the abscess may be fairly regular or much eroded, and the pus may be seen to be invading it in deep bays, or long tubular-like processes, which often run parallel to the long axis of the main cavity from which they spring. The extension of the suppurative process, leading to the formation of larger abscesses from the running together of smaller ones, can be easily traced. Papillary-like septal processes can often be seen stretching into the cavities, and sometimes small islands of septæ remain lying free in the pus. The walls separating the abscesses vary in thickness as much as the abscesses do in size, being sometimes of much smaller, sometimes of much greater breadth, than the abscess cavities they separate. Their structure is that of a fine reticulum of fibrous tissue, with many large, rounded, spindle-shaped, or greatly elongated connective-tissue cells. A few leucocytes are generally to be seen in the fine meshes at the abscess margin. This reticulum is often formed of extremely slender threads, which gradually thicken as we pass away from the margin, the cells diminishing in numbers at the same time.

It may thus reach a considerable degree of density, consisting of bundles of thick, wavy, parallel fibres, with long spindle-shaped and rounded cells. This arrangement is often seen between two abscesses, and generally its position suggests a capsule-like structure bounding each individual abscess. In many places, in the process of the extension of the abscess, the

more delicate parts of the walls have been destroyed, and the pus has come into contact with the denser parts.

This fibrous tissue is vascular, the blood vessels being generally rather scanty, though in a few parts they are numerous. They are always rudimentary, showing little beyond a layer of endothelial cells, sometimes proliferating somewhat, lying upon a delicately-fine threadlike fibrous layer. Their usual contents are red blood corpuscles, with now and then a few leucocytes. No abnormal constituents can be seen in them. There may be much or very little reticular tissue between an abscess cavity and the liver cells; different parts of the growing margin showing this very well. It is seen to be continued into the liver substance as an intercellular cirrhosis. There is hardly anything like a line of demarcation to be seen, although the intercellur cirrhosis gradually becomes finer as we pass deeper in among the liver cells. At first the round and spindle cells of the reticulum are seen to be regularly replaced by the greatly altered liver cells. They are sometimes flattened and much elongated and with difficulty distinguished from the connective-tissue cells; at other times they are angular and irregular. The blood vessels of the reticular tissue seem at places to be continuous with the intercellular capillaries. Besides this intercellular cirrhosis there are dense bands, sometimes passing continuously from the abscess margin into the liver substance, and at other times seen as isolated areas within it. They clearly represent portal spaces, in which a marked cirrhosis has taken place. This is so constantly present within the near proximity of the margins of the invading growth as to suggest a monolobular arrangement. While the connective tissue of the portal space is greatly increased, there are other alterations to be observed. The bile-ducts retain their columnar epithelium, and appear to be considerably increased in number; moreover, isolated bile-ducts are not infrequently noticed in the denser parts of the reticulum, showing that they are the last of the structures of the portal space to disappear. The hepatic artery may show an endarteritis obliterans, and generally it, as well as the portal vein, which may also show some proliferation of its

endothelium, is difficult to detect. The liver cells are atrophied, fatty, both nucleus and protoplasm being often vesiculated. An abundant golden yellow pigment is frequently present throughout the protoplasm of the liver cell which, while it seemed to resemble an iron pigment, gave no iron reaction with ammonium sulphide or with ferrocyanide of potash and hydrochloric acid. This pigmentation was seen to be most extensively distributed throughout the liver, immediately around the abscesses as well as in the connective-tissue cells of the growth itself. A slight congestion of the interlobular capillaries is frequently seen towards the outskirts of the intercellular cirrhosis.

While this description represents what is seen generally throughout the growth, yet other and equally interesting appearances are observed. At many places in the reticulum of the abscess walls, in the neighbourhood of the liver substance, small rounded or oval spaces are seen. These are occupied by small actinomyces colonies, mostly some modification of the oblong form, showing both filaments and clubs. The margin of the colony is closely surrounded by a number of elongated spindle-shaped or fusiform connective-tissue cells, with here and there a leucocyte between. These are at first closely packed and radiate outwards in the same manner as the filaments and clubs, becoming fewer as the margin of the space is reached where one or more giant cells appear. The giant cells vary greatly in size, are rounded, oval, or irregular in shape, with a definite outline and a varying number of nuclei, generally arranged in a group at one end of the protoplasm. Among the giant cells there are also a few leucocytes and connective-tissue cells. The margin of the space shows elongated connective-tissue cells, somewhat concentrically arranged, between which the fine reticulum speedily appears. Further, large giant cells, one or more may be seen immediately surrounding a part of the colony, replacing the above-mentioned connective-tissue cells. Such giant cells may be crescent-shaped, with a well-marked ring of nuclei towards their outer convex border, or they may be very large irregular-shaped bodies surrounding some of the outlying portions of the colony. Their protoplasm may be

homogeneous or granular, and their nuclei may be very numerous, arranged in the centre or at one end, not peripheral as in tubercle. Similar actinomyces follicles are also seen here and there at the margins of the abscesses. Again, giant cells are seen lying, either singly or in groups of two or three, in meshes of the reticulum, especially in the neighbourhood of the follicles. A few of the giant cells show little banana-like bunches of clubs within their protoplasm, like the one seen in Fig 10—in which a colony or colonies occupy more than three-quarters of its protoplasm, while its nuclei, five or six in number, are seen crowded together at one end. A part of these enclosed colony or colonies consist of bunches of clubs apparently without filaments, while another part shows both clubs and filaments.

Such a condition is extremely rare in man, although not infrequent in the ox. So far as I have been able to discover it has not yet been described as having been observed in man. I did not succeed in discovering any of these actinomyces follicles in fibrous tissue, where the liver cells could still be detected, nor indeed any trace of their extension into any part of the liver beyond that. It would thus appear that the parasite first induces a diffuse cirrhosis in the liver, and, as this cirrhosis tends to take a fine intercellular distribution, that the virus is probably distributed by means of the intralobular capillaries. From the denser nature of the fibrous tissue in the portal tracts, it would also appear as if the virus was first of all spread by one or other of the structures contained in these tracts, leading to a monolobular cirrhosis, and that, for a time at any rate, it did not begin to invade the lobules themselves. We have already seen that the bile-ducts retain their epithelium, and that, beyond a probable increase in number, there are no indications to show that they are involved; while, on the other hand, the branches of the hepatic artery, and also to a less extent those of the portal vein, show signs of an irritation in the desquamation and proliferation of their endothelium, which leads to the suspicion that the virus may have spread by these channels. It is extremely difficult to make out the margin of the adventitia of the hepatic artery branches, as it is merged with the thickened fibrous growth around it in the

portal tract. I could not make out any lymphatics, and am therefore unable to speak of them. After the monolobular cirrhosis has advanced some distance it invades the substance of the lobule, producing an intercellular cirrhosis. The results of the action of the virus are obvious enough, but its nature is not so. Two alternatives suggest themselves—(1) the action of some early form of the actinomyces or other accompanying organism, which precedes the lesion, as suggested by Samter.[1] He thinks that threads or bacilli first appear, and after setting up an inflammation, again disappear without further development; (2) the effect produced by the bacterial excretions formed at a distance and distributed throughout the part.

After a most diligent search for organisms in the vessels of the portal spaces, the intralobular capillaries, the central and sublobular veins, and hepatic lymphatics, I did not succeed in finding any, except a number of micrococci in a few of the capillaries and sublobular veins. One or two of the latter were, however, quite filled with plugs of micrococci, even at considerable distances from the invading margin of the growth. These micrococci are of much the same size and character as the cocci seen in the actinomyces colonies, and there is a possibility that they may have taken their origin from them. From these observations the following conclusions seem probable:—(1) The excretions of either the actinomyces or accompanying germs or both are widely distributed throughout the immediate neighbourhood, and in advance of the actinomyces itself, leading to a formation of fibrous tissue, the arrangement and distribution of which will depend somewhat upon the structure of the tissue invaded, but with a tendency towards the formation of a reticulum. (2) The actinomyces follicles sooner or later appear in this fibrous tissue. (3) The follicles become the seat of small abscesses, which, by extension, open into one another.

While the follicles vary somewhat in detail, they are all built upon the same plan. The colony occupies the centre, and around it are large connective-tissue cells, arranged with their long axes perpendicular to the periphery of the colony. Towards the margin, one or more giant cells appear; and,

[1] *Archiv für klin. Chir.* 1892. Bd. xliii. s. 316.

outside them, the connective-tissue cells are now arranged with their long axes, tangential to the margin, and, joining one another by their ends, form a number of concentric lines like a capsule around the follicle. Leucocytes may be present in small numbers among the other cells. Later, the leucocytes generally, though not invariably, multiply greatly so as to distend the follicle, whose walls gradually undergo at the same time some liquefying process, and thus an abscess cavity results. Various stages in the transformation of the follicles are to be seen. They may remain apart, or open into one another, and occasionally an abscess is seen invading a follicle in which no abscess formation has yet taken place. The resemblance of the follicle of actinomycosis to that of tuberculosis is too striking to require to be pointed out. It has been discussed by Samter,[1] who regards them as almost identical in method of production and structure. He and others have recorded 1 or 2 cases of combined tuberculosis and actinomycosis, but, so far as I can find, in none of them were the specific organisms of both diseases demonstrated to be present. In his paper, page 294, Samter mentions that in his case staining for the tubercle bacillus gave negative results. In the absence of such proof we cannot regard the combination as proved. His comparison between the two diseases is restricted, and leaves many interesting points unnoticed; moreover, I am not able to agree with him entirely. The question is an interesting one, but I shall content myself with a mere passing reference to some of the more interesting points I have observed. The parasite in both diseases reacts upon the tissue cells, converting them into epitheloid and giant cells; in both it is found within the giant cells; in both there is a great tendency for accompanying organisms to set up irritative conditions, leading to abscess formation, and more or less masking the changes proper to the parasite itself. These typical actinomycotic follicles are the common manifestations of the disease in the ox, where abscess formation is rare; but in man, on the other hand, they have been rarely seen. In the disease in man abscess formation is constant, and moreover would seem generally to occur with too great rapidity to

[1] *Archiv für klin. Chir.* 1892, Bd. xliii. s. 345, 346.

allow time for the formation of typical follicles. In nearly all the cases recorded, in which the position of the colonies has been described, they are seen bathed in and surrounded by pus. This has led many observers to hold that the actinomyces is itself a pus-producer, and ought therefore to be included among the small number of the pyogenic organisms. There is no doubt whatever that it can live, increase in size, and multiply within the pus, but this merely shows that pus is a suitable nidus. The same difficulties at one time surrounded the action of the tubercle bacillus. Observers were puzzled to account for the apparent multiplicity in the form of lesions produced by it, until they learned to discriminate between the results of the action of the bacillus when pure, and when mixed with other organisms. Considerable differences of opinion exist even yet upon the question. There is a difficulty in pushing the parallel too far, as, while the specific actions of the tubercle and actinomyces organisms resemble one another in their formative reaction upon the tissue cells, yet there is nothing comparable in the latter with the destructive action of the former. There is no hyaline or coagulative necrosis or caseation which follow so rapidly upon the formative action in the case of the tubercle bacillus. It is further instructive to observe that the two organisms present a striking difference in their relation to lymphatics. The lymphatic glands are favourite and common sites of tubercle and the lymphatic channels its usual method of spread; while there is practically no evidence to show that actinomyces ever affects lymphatic glands, or even spreads by the lymphatic vessels. Observations by various observers render the latter a likely enough presumption, but, on the other hand, such great authorities, as Boström and Samter failed to find any evidence of it. In actinomycosis the formative reaction is probably slow, and produced by a slowly growing actinomyces. When other organisms, like the streptococcus or *Staphylococcus pyogenes aureus*, find a lodgment in the follicle, the suppurative process is set up. The greater rapidity of growth which is then seen in the actinomyces itself may be due partly at any rate to some of the accompanying organisms using up the free oxygen around it, as it is

naturally an anäerobic organism, although it is facultatively an äerobic one. Observations made by Bostion[1] show that in certain parts of the body actinomyces may develop without the presence of pus. I am, therefore, inclined to believe that it is not a pus-producer, that its action is mainly of a formative and not of a destructive kind, and that the destructive lesions so commonly seen in actinomyces are due to one or other of the accompanying organisms. Streptococci or staphylococci were seen to be present in this case, and have been noticed by several observers in others. It is difficult to determine what part these and other accompanying organisms play in the process. Many of those I have described are doubtless post-mortem intruders with no pathogenic influence, but it is at least probable that all of them are not so. It is of course possible, even if they are not all of post-mortem origin, that they are of accidental occurrence, and without influence upon the changes and variations seen in the actinomycotic lesions, which would thus require to be referred to the action of the excretions of the actinomyces itself. There are many such instances of great differences in bacterial action in the tissues of the same animal, referable apparently to varied conditions of environment. It is obvious enough, for instance, that variations in their food supply and conditions of development will materially affect the excretions which the bacteria produce. Thus we have the *Staphylococcus aureus*, at one time the cause of ulcerative endocarditis, and at another of acute osteomyelitis; the *Streptococcus pyogenes* of such diverse lesions as ulcerative endocarditis, abscesses, erysipelas, or even pernicious anæmia, if we accept the recent observations of Fischel and Adler.[2] It may be then that the amount and virulence of the excretions produced by the actinomyces under different circumstances are alone responsible for the varying lesions seen in bovine, equine, and human actinomycosis.

The colon.—Parts of the wall were selected near the lesion in the liver, and others at a little distance from it. The latter show small elongated abscesses situated in the submucous coat. These lie with their long axes parallel

[1] Boström, *Verhandl. d. long. für innere Med.* p. 94. Wiesbaden, 1885.
[2] *Zeitsch f. Heilk.* 1893. Heft 4.

with the mucous membrane. They are sometimes situated just beneath the muscularis mucosæ, at others somewhat deeper, or even close to the circular muscular coat. Occasionally a small abscess is seen in the mucous membrane, having been apparently formed just beneath the muscularis mucosæ, and, having ruptured it, extended among the Lieberkühn's follicles, destroying them until it almost reaches the lumen of the intestine. The structure of these abscess cavities and their walls closely resembles that already seen in the liver. Actinomyces colonies of various size and form are seen lying in the pus. The typical filaments are well seen in them all while some of them also show clubs. In one old colony of an oblong form, the filaments are much degenerated, cocci and bacilli are extremely numerous, while some of the clubs are large and of the palmate or fan-shape form. This colony, moreover, is not in the centre of an abscess cavity, but is surrounded by a well-formed reticulum, showing large connective-tissue corpuscles and a few doubtful giant cells. The circular muscular coat of the intestine is here much thinned, but in other places does not seem to be affected. The peritoneal and longitudinal muscular coats are unaffected except in so far as they contain micrococci, streptococci, staphylococci, and various bacilli in immense numbers. The mucous coat is fairly healthy, showing little except a shedding of the surface epithelium, and some atrophy of the cells of Lieberkühn's follicles.

The lesion is thus seen to lie chiefly in the submucous coat, involving the mucous coat occasionally by small areas, which may serve to discharge the pus into the intestinal canal. This is shown in Plate II. Fig. 5. This discharge must be favoured by the intestinal peristalsis, and might lead in this way to the complete extrusion of the parasite, which might thus be detected in the stools. This has actually been done by Ransom.[1] A healing process would then probably ensue, resulting in the formation of pigmented and depressed cicatrices. Such cicatrices have several times been seen by observers, *e.g.* Israel,[2] and tentatively referred by them to

[1] *Royal Med. and Chir. Soc. Trans.* 1891.

[2] *Virchow's Archiv.* 1885. Bd lxxxvii., lxxxviii.

healed actinomycotic foci. Such a result is here seen to be probable. The lesions lie comparatively superficially. They consist chiefly of abscesses, which are seen at intervals to reach the lumen. The tissue between the abscesses is mostly a fine fibrous tissue, arranged like a network, and considerably more muscular than it appeared in the liver; but in places it is of considerable density, showing the tendency to cicatrisation often seen in actinomycotic areas. It is interesting to note that beyond a slight pallor and thickening, there were no-naked eye signs of the presence of these abscesses. The mucous membrane looked healthy. In a case of primary actinomycosis of the large intestine, described by Chiari,[1] there were several white raised patches about $\frac{2}{5}$ in. diameter and $\frac{1}{5}$ in. thick, firmly adherent to the mucous membrane, and showing many yellow actinomyces granules, while the mucous membrane around them was swollen and red, and covered with a thick layer of tough mucus. In other cases the condition was similar to that seen in this Case, viz. a general, thickened infiltration of the mucous and other coats. Comparing the sections just described with those taken from the more diseased part of the colon, it is seen that the mucous membrane is gradually lost, that abscesses with contained colonies are seen, chiefly in the submucous coat, as before, that the muscular coats are not at first involved, whereas the peritoneal one becomes much thickened. Soon the muscular coats become atrophied and disappear as the part adherent to the liver is approached, when the wall presents no trace of colon structure, simply showing abscesses surrounded by fibrous tissue. As this was the part in which the disease first appeared, extending to the liver after it had been bound to the colon by inflammatory adhesions, there was unfortunately in it no trace of the early stage left. The appearances presented by the wall of the colon for some distance from it show how, once it finds a lodgment in the submucous coat, it tends to extend longitudinally along it, leading to a destruction of the mucous coat. Therefore the changes present in the intestinal wall at some little distance away, which I have

[1] "Ueber primäre Darmactinomycose beim Menschen," *Prag. med. Woch.* 1884, No. 10.

described above, probably show the early conditions produced by the parasite after its invasion, although they do not determine its exact mode of entrance. So far as the general peritonitis is concerned, there was nothing to show that it was of actinomycotic origin. The *Streptococcus pyogenes* and *Staphylococcus aureus*, but not actinomyces, were found in the lymph and pus, and it must have been of independent origin, from the septic wounds communicating with the abdominal cavity or from the gangrenous colon.

The spleen.—Beyond showing considerable congestion of the pulp, especially beneath the capsule and around the superficial Malpighian bodies, this organ is quite normal. A few of the small venous sinuses are seen, after staining by Gram's method, to contain a number of micrococci and short streptococci, but no other organisms.

The right kidney.—The capsule showed a considerable patch of fibrous thickening with large blood sinuses in it. This is the area referred to on page 16, as seen with the naked eye. There is no sign of any actinomycotic lesion here. It is apparently of the nature of a fibro-vascular growth. Beneath this thickened capsule the superficial cortex shows a large area, in which the structure closely resembles that of a tubular angioma. The intertubular capillaries are greatly dilated, all traces of the tubules having disappeared, except towards the periphery, where their remains gradually reappear. No traces of glomeruli are seen in the centre of the area, while those near the periphery and in the neighbourhood are quite healthy, except for slight local dilatations of their capillaries, as are also the others throughout the kidney. Other smaller patches of similar congestion are seen near this one, and close to the surface. They are irregular in size, outline, and depth. Their greatest breadth is generally towards the capsule. A few of them show remains of the compressed convoluted tubules in their midst, and towards their peripheries they show their formation clearly, the intertubular capillaries being have only slightly dilated and the gland tubes little altered. A gradual transition from a simple congestion to a fully-developed tubular angioma is seen. There is no hæmorrhage into the gland tubes themselves. This kidney condition is

thus of accidental significance. The convoluted tubules of the cortex generally show some swelling and slight desquamation of their epithelium, and a few of them contain casts of a somewhat hyaline appearance, apparently derived from the desquamated epithelium. There is no increase in the connective tissue of the cortex. The straight tubules and the vessels of the medulla are practically normal. Micrococci and streptococci, similar to those in the spleen, are present in some of the larger vessels and capillaries.

The left kidney shows nothing of note except some swelling and desquamation of the epithelium of its convoluted tubules.

The vermiform appendix and tissues around.—A section was made, involving a transverse section of the vermiform appendix, about ¾ in. from its apex, the fibrous tissues in its neighbourhood and the inner wall of the ascending colon attached thereto. This showed many interesting conditions, but I shall only mention that the blood vessels in the adhesions around the vermiform appendix were mostly crammed with micrococci, staphylococci, and short streptococci, that a lymphatic gland lying in the adhesions between the appendix and colon showed similar organisms within and around its capsule, but no actinomyces, that the mucous and muscular coats of both appendix and colon were but little affected.

Microscopic examination was also made of the other organs of the abdominal cavity, including the stomach, duodenum, pancreas, bladder, prostate, and mesenteric glands, with negative results. The mesenteric gland, already referred to as the seat of an abscess, showed an acute lymphadenitis; no actinomyces was found in it.

The lungs. — There are general and widely-spread changes to be seen throughout, but the bronchioles and small-sized bronchi, show the most characteristic change. They are all the seat of an acute or subacute bronchitis. Their ciliated epithelium is shed, and is seen to lie within the pus, which, in most cases, fills the lumen and contains one or more actinomyces colonies. The blood vessels of their walls are much dilated. The lung parenchyma around them shows little or no change, or, as in a few of the smaller ones, a

small area of catarrhal pneumonia. The lung alveoli generally contain a few large uni-or bi-nucleated catarrhal cells, with or without carbon and other pigment particles. They often also show a good many red blood corpuscles close to the alveolar septa, and granular material within the alveolar cavities. The alveolar septa are pretty generally a little thickened, sometimes considerably so, their lining epithelium swollen in places, and their capillaries fairly normal. The interlobular septa show occasionally an increase of fibrous tissue, and there is a distinct area of catarrh and collapse along the line of one or two of them for some distance. There are scattered and collected masses of black pigment at intervals along them. These changes are mostly of a chronic nature, and are sharply distinguished from the more acute condition of the bronchi and bronchioles. The pleura also shows an acute inflammation, the blood vessels of its deeper layer being much dilated, and a considerable quantity of lymph thrown out upon its surface. The underlying lung tissue shows a slight catarrh, and a considerable exudation of leucocytes into some of the alveoli. There are here several distinct abscess cavities, but none of them show actinomyces colonies. As already observed, the most characteristic changes are seen in the smaller bronchi and bronchioles, and of the two the former seems the more affected. Their walls vary considerably in thickness throughout. The outer coat is least altered, its blood vessels being dilated, sometimes extensively, leucocyte infiltration being varied in amount and generally scanty, and the cartilage plates, when present, slightly atrophied or unaltered. The submucous coat shows much dilatation of its vessels, many running in loops towards and penetrating into the mucous coat; the mucous glands are seen to be slightly cloudy, and there is a scanty leucocyte infiltration around them. The mucous coat shows the most extensive changes. Its muscular layer is well seen in places, but is often atrophied, and sometimes penetrated by the invading vascular loops of the submucous coat. The fibrous part is somewhat scanty, its elastic fibres having largely disappeared. The lumen is most imperfectly lined by a few irregular or rounded cells, absent in places, so that the fibrous

or muscular tissue comes to the surface. The natural ciliated columnar cubical epithelial lining is completely shed, and is seen to lie scattered everywhere in the pus, which fills the cavity. These epithelial cells are frequently still adherent to one another, as many as nine or ten can sometimes be counted in one cluster. They retain their outlines clearly, and their protoplasm is somewhat granular, but stains fairly well, and is otherwise little altered. Their nuclei have mostly lost some of their chromatin substance, but can all be made out with ease. The cilia are as clearly seen as in the normal condition. In some cases, however, especially in some of the bronchioles, the shed epithelium is somewhat broken down, and shows a tendency to fuse into indistinct masses without nuclei. They lie in the pus, which appears to be more abundant in the smaller bronchi than in the bronchioles. The pus is composed of altered leucocytes, with a few connective-tissue cells. No distinct fibrous tissue of any kind is seen within the lumen, in or around the pus, such as was described and figured by Hodenpyl [1] in his two cases of pulmonary actinomycosis. Actinomyces colonies are seen lying with the pus. They are of various sizes and ages, and of different growth forms, often grouped together. Many of them are pigmented. In the larger bronchi they lie bathed in the pus, and do not seem to be in any way related to the shed epithelial cells, but in some of the smaller ones they come close up to the walls, and their filaments appear to penetrate the wall, while the epithelial cells lie close to them. They show the typical filaments abundantly and well, many cocci in places, and occasionally young clubs, which are, however, somewhat scanty and slender. One of the larger bronchi has been represented in Plate III. Fig. 6. In the neighbourhood, and at distances from the colonies, short or long threads, and small groups of cocci, with one or two short filaments growing out from them are seen; while a few cocci, short rods, and bits of threads are here and there seen within the pus cells. An interesting feature is the comparative paucity of the actinomyces colonies, *e.g.* one piece of lung tissue, measuring $\frac{7}{8}$ by

[1] *New York Medical Record*, 1890, pp. 654, 655.

§ in., shows in some of its sections six colonies only, and in others four. These colonies are thus distributed. Five lie in the largest bronchus seen in the section, and one in a small bronchiole with but few pus cells around it; the wall of the bronchiole itself being incomplete at one part. There are several other bronchi and bronchioles in the section containing pus without colonies. A few other sections of this same piece show three colonies in the same large bronchus, one in one of the larger ones, and one in the same small one, while numerous other sections show two or three in the two largest bronchi, but none in any of the others. Again, a few colonies are observed in the alveoli, free from pus and more or less filling the alveoli, whose walls seem quite normal. Ciliated columnar epithelial cells are often also seen to lie in the alveolar cavities. One or two pieces of lung had section after section cut, without showing a single colony, and others only showing one occasionally. All of them, however, showed the same chronic and acute catarrhal and inflammatory changes, and all of them showed large numbers of micrococci, streptococci, and staphylococci, both in the vessels of the pleura and lung substance, and in many of the bronchioles and bronchi. It is thus seen that the largest bronchi which my sections showed, contained the largest number of colonies. This can be explained either on the supposition that this was their primary seat of formation and habitat, or that they had collected there on their way upwards from the bronchioles; but, from the very small number of bronchioles and alveoli, not more than a few, in dozens of sections, which showed any colonies, the former view would seem to be the more probable. This points to a primary bronchitis as the manifestation of the actinomycotic lesion in the lung; further, the changes are here seen to be of an acute character, and to show no sign of the reticular and fine fibrous tissue formation already observed in the liver and intestine. The limiting part of the bronchial wall shows an appearance in places which might be construed as representing this reticular tissue, but it may be, when the process is so acute as this, that the formation of fibrous tissue is prevented by the rapid production of pus, the result of a mixed infection, in which

other organisms manifest their presence sooner than the actinomyces. A large colony, apparently of some age, is seen in the midst of one of the collapsed areas in the lung. It does not appear to have caused any change in its neighbourhood, and yet its presence, in completely collapsed lung tissue, probably indicates that it has been there for some time.

The heart.—The pericardium and endocardium are normal, while the myocardium shows a somewhat advanced fatty degeneration.

The bronchial glands and thyroid were also examined microscopically, but showed nothing worthy of note.

Biological position of the actinomyces.—This case presents many favourable opportunities for the study of the relationship of the different elements, viz., filaments, cocci, and clubs to one another. Many of the colonies are seen to possess all three, in many others clubs are entirely absent, while in a few (if we are to regard the small banana and rosette-like branches as separate colonies), they are apparently the only element present. (1) The filaments.—They are constantly present in man, and probably in all the colonies. They are always seen to the best advantage in the actively growing colonies, in which they form threads with continuous and homogeneous protoplasmic contents.

In the older colonies, or in others whose growth has been interfered with, an interruption of the protoplasm is observed. The form which this most usually takes is that of a string of streptococci, which thus appear to be contained in a fine capillary tube. These round or slightly oval segments are sometimes closely crowded together within the tube, sometimes at considerable intervals apart. At first they are of much the same character as the tube in which they lie, but presently an inequality appears, the segments apparently increasing in size, and the walls of the tube shrinking, so that the appearance comes to resemble that of a string of beads. They generally continue to show remains of the walls of the tube, but in a few instances no such remains can be traced, and the segments then resemble ordinary streptococci in their arrangement. Completely empty tubes are rarely seen, but partially empty ones with free cocci near them are not in-

frequent. Again, in many of the older colonies, and in those whose growth has been retarded, an opposite irregularity of diameter between the tube and its contained segments appears, inasmuch as the latter appears to shrink instead of increase in size, so that we now see an appearance of small, differently-sized, often angular segments within a slightly withered-looking tube. This difference in behaviour suggests some essential difference in the significance of the two processes. The first looks like a vital process of importance in the further development of the colony, while the latter is more like some degenerative change ushering in its death. The larger segments, the cocci and streptococci, resemble active and growing products of the protoplasm of the filaments, while the smaller even more closely resemble its degenerated and dying remains. Both class of segments stain much in the same way, the smaller ones showing but little diminution in their affinity, for all the dyes absorbed by the larger. The very small ones, however, show less intensity of stain, and from their shape and their other appearances, I am of opinion that they are merely signs of degeneration and death occurring in the colony. The larger cocci-like segments are more difficult of explanation. They stain with the same intensity as the unbroken protoplasm of the filaments, and their appearances and formation suggest that they are spores produced by terminal extrusion from the filaments, or by lateral disruption of their walls; a suggestion which their method of development and staining reactions, so unlike those proper to spores, make it difficult to accept. (2.) The cocci.—They are present in all except the small and young colonies. After a filament comes to be of a certain age, it would appear to produce cocci, and perhaps also short bacilli, which, becoming massed together form the older and denser parts of the colony, while the ends of the filaments continue to grow and radiate outwards as the peripheral threads. In no case did I find many free cocci among these peripheral threads towards the margins of the younger colonies in either the liver or colon, and all or nearly all of such as were seen are probably only the ends of filaments running perpendicularly to the section; but in the lung they

were more numerous. In a few instances, one or more large closely-packed shrub-like outgrowths of filaments, similar to those referred to on page 144, and figured in Plate IV., Fig. 8, had become entirely converted into cocci. I cannot say that I found any colony entirely made up of cocci, although a few small ones in the lung appear to consist of a small number of cocci giving rise to a few short filaments, while separate cocci, lying side by side with short bacilli, suggest the probability of the evolution of the latter from the former. (3.) The clubs.—Of almost constant occurrence in the ox, they are comparatively infrequent, though not uncommon in man. Among the English cases, for example, they were seen in Eve's, Delépine's, the Brompton, Taylor's, and a few even in Acland's case, according to Crookshank, who held that they were present in all cases. They are found at the margins of certain of the colonies, others showing no signs of them. They stain similarly to, but more intensely than the ground or fungous substance of the colonies, but show considerable variety in the depth of their colouring, the young ones being much darker than the old ones. M'Fadyean[1] also refers to the variation in the staining of the clubs according to their age. As they are present in young as well as old colonies, they seem to be an indication of retardation or arrest of growth rather than of age. This opinion is also held by Boström, Paltauf, Delépine, and others. We must remember also that the arrest of growth which naturally follows upon age might be induced prematurely by various conditions of environment. Delépine had a favourable opportunity for observing that clubs probably did not appear until after a colony was five or six weeks old. This was under ordinary conditions of growth. It is therefore possible that under inhibiting influences they would appear earlier. This may account for their presence in the young colonies in this case. They are seen lying among, and usually reaching further out, than the ends of the filaments, which, in a few instances only, I observed to penetrate into them. In these instances, the filament formed a central core within the club, its protoplasm usually showing interruptions, with the terminal

[1] *Journ. of Comp. Path. and Therap.* 1889, vol. ii. p. 16.

segment not visibly increased in size. This intimate relationship between the filaments and clubs has been conclusively demonstrated by many observers, and effectually silences the objection that they are merely two different organisms, accidentally superimposed upon one another. I am not certain that I can trace in my specimens all the steps in the formation of the clubs, but there is enough evidence to show that they are the result of a thickening of the sheath of the filaments. Many observers, among others, Ponfick,[1] Israel,[2] Crookshank,[3] Boström,[4] and Bollinger,[5] have clearly demonstrated this, and all authorities are now practically agreed upon the point; but, while there is a general consensus of opinion regarding their formation, conflicting views are held as to their significance and relationship to the processes of development of the organism.

According to one view, they are to be regarded as organs of fructification, while, according to another, these are merely involution forms, indicative of a degenerative process. The question is an important one, as its solution will decide the true botanical position of the actinomyces, whether it is to be considered as one of the true fungi or as one of the bacteria. It may be approached from two sides, firstly, by a careful study of the morphology of the organism, and, secondly, by tracing the stages in its life-history and development. For this purpose I attempted to cultivate it artificially. Separating some of the actinomyces bodies carefully from the pus taken from some of the abscesses lying within the deeply-situated growing margin in the liver, I washed them thoroughly in distilled water and inoculated them both upon the oblique surface and deeply into the substance of agar-agar. Ordinary agar and 5 per cent. glycerine agar were both used. A temperature of 37° C. to 37°·5 C. was employed, under aërobic conditions, and the cultivations were examined daily. No change whatever at the inoculation

[1] *Die Actinomykose des Menschen.* Berlin, 1882.
[2] *Virchow's Archiv*, Bd. lxxiv. p. 18.
[3] *Med. Chir. Trans. Lond.* 1889, and *Text-book of Bacteriology.*
[4] *Loc. cit.*
[5] *Centralbl. für d. med. Wissen.* 1877, No. 27, and *Deutsche zeits. für Thiermedicin*, 1877, Bd. iii.

points or lines could be observed with the naked eye during the first five days. With the aid of a small hand lens, very tiny clear-looking spots were observed along the whole line of the needle track in the deep culture. These grew larger very slowly, and on the seventh day could just be observed with the naked eye. They did not run together. Similar points appeared on this day on the surface cultivations when examined with the hand lens. They gradually, but slowly, increased during the next few days, becoming faintly white. Those within the substance of the agar continued to be larger than those upon the surface. From the thirteenth to the fifteenth day the largest were about the size of pin-heads, while others were a little smaller. The former gradually became more opaque, especially in the centre. They were round or oval, with a firmly-crenated or nodulated exterior. After three weeks a few of them assumed a slight yellow colour, seen upon the surface and also especially when held between the observer and the light, and examined from below. They increased very little, if at all, in size after this period, and showed little or no tendency to fuse together in their growth. They were extremely tough, tenacious, and hard, and it was practically impossible to detach any part of them with a needle, the whole of a nodule having to be scooped out with a little of the agar. Those upon the surface grew upwards, looking at first like little upstanding clear drops. Later on, as they became somewhat opaque, they grew slightly downwards into the agar, so that a small part of each little mass lay beneath the surface. This did not appear to be a continuous growth of the whole under surface, but of separate little root-like processes. As I found that the glycerine agar was the more suitable medium, I inoculated fresh tubes from the first, and repeating the process, obtained three generations resembling one another closely in growth. I may mention that only two of the first generation cultures corresponded in full detail to this description, the others showed growths at much earlier periods and were rejected, as microscopically they were seen to be very impure. Some of the second and third generations likewise failed, and I thought it advisable to try the effect of needle-stroke cultures taken from the third generation.

Although I tried this more than once, no growth whatever, so far as I could discover, appeared, and while attempting to find an explanation of this I was unfortunate enough to have my cultures accidentally destroyed. I had meanwhile made cover-glass preparations of all three generations at different times. I had the disappointment to find that none of them were actually quite pure, and hence I shall confine myself to a brief description of the main stages shown in what I am convinced represents the growth of the actinomyces itself. An eight-day old culture showed a large number of short bacillary forms, straight or slightly curved, sometimes slightly larger at one extremity, single or in pairs or placed end to end in short chains. The elements in these chains were not of equal length, most had one axis larger than the other, but a few were almost isodiometrical. These chains were straight, wavy, or sharply bent, and rarely there was an appearance of short lateral branches. They were scattered all over the field as well as grouped closely together, but did not show any radiate arrangement. The appearance is seen in Fig. 11. An eleven-day old culture showed a profuse development of filaments, forming an abundant network, sometimes showing a tendency towards the formation of a radiating colony. The central part of such a group consists of fine filaments, closely resembling those of actinomyces, as already described, interwoven and interlacing with one another, and giving off long or short wavy filaments which radiate outwards. At other parts they form a close or open felted mass, or lie apart from one another. Branching is present, the dichotomous variety being rare. The filaments themselves frequently show an interrupted protoplasm, and there are enormous numbers of micrococci lying among them. Fig. 12 gives a view of this culture. A fifteen-day old culture shows similar filaments less densely arranged, sometimes very short, sometimes of great length, wavy, bent, or spiral, and with a much interrupted protoplasm. Their resemblance to tubes is now very great, and the contained protoplasmic segments vary considerably in size, a very few being elongated, but most being rounded. Sometimes the end of the tube has a well-marked, deeply-stained bulbous swelling. This is represented in Fig. 13. Staining with Gram's method and

eosin causes the walls of the empty tubes between the contained cocci to appear of a pale pink colour, while the cocci themselves are a deep blue. No clubs or any traces of them were seen in any of the many cover-glass preparations examined. The deductions which can be drawn from these observations are:—(1) the filaments give rise to cocci like forms, either by terminal extrusion or lateral disruption; (2) these cocci forms grow out into short bacilli; (3) these short bacilli become placed end to end and fuse to form a filament, or grow out uninterruptedly into a filament; (4) clubs are apparently unnecessary in any of these processes. In forming conclusions regarding the value of these observations it must not be forgotten that the cultures were not pure. Moreover, another objection is possible, viz., that the microscopic appearances observed are due to a part of the originally implanted actinomyces and not of a third generation at all. The latter objection is, I think, sufficiently refuted by the naked-eye appearances of the cultivations. Boström in his most valuable and elaborate paper, already referred to, gives an excellent and very full account of his own culture results. He made cultivations in series (about 700), from eleven cases of bovine actinomyosis, and also others from five cases of human actinomyosis. Three of the latter were successful. He used gelatine, agar, bouillon, and potatoes, as his nutrient media, and carried on his cultivations at a temperature of 37° C., under both äerobic and anäerobic conditions. His results are in many respects different from those obtained by me. He observed little, clear, dewdrop-like bodies becoming white in the centre after, forty-eight hours, or even earlier, while a thin, grey, moist appearance had been seen along the line of inoculation even before that. The little bodies then rapidly increase in size until they form little masses, larger than pin-heads, becoming at the fourteenth day of a yellowish-red or a clear brick-red colour, the central part being darker and more prominent, while the margin is irregular. When microscopically examined his cultures of twenty-four hours consisted of abundant filaments, interweaving and branching, and showing a homogeneous protoplasm. During the second day they became denser, and on the third and afterwards, showed numerous short bacillary and coccus forms, both in and

outside the filaments. Many cocci were seen lying in rows alongside empty filaments. In the deeper layers of his blood-serum cultures clubs were frequently found. He believed that they only appeared when the nutrient material was exhausted. They soon perished or became calcified, but never vegetated, even when their contained filaments continued to grow. His inoculations on animals were not successful. The conclusions he has drawn from his investigations are—(1) the cocci are the spores of the organism; (2) they grow out into short bacillary forms; (3) these bacillary forms grow out into filaments; (4) the clubs are due to degenerative changes in the sheaths of the filaments and are not organs of fructification; (5) therefore, the actinomyces is a cladothrix form of bacterium. This investigation of Boström's, admirable though it be, yet leaves room for doubt; for it is to be noted that he does not claim to have worked with pure cultures, and it may even be asserted, as has been done by Afanassieu,[1] that the cocci and bacilli are the products of contamination, while the dichotomously-branched threads are merely the visible remains of the inoculated material.

Protopopoff and Hammer[2] also differ from Boström in so far as they found dichotomously-branched threads in a fourteen-day old glycerine-agar cultivation, and no bacilli or cocci until after an interval of one to one and a half months.

Wolff and J. Israel[3] still more recently have made a most important contribution to this subject. They took their material from 2 cases in man, and used agar-agar and egg albumen as the nutrient media, at a temperature of 36°·5 to 37° C., both under anäerobic and äerobic conditions. The results obtained by me closely resemble theirs. The aneärobic cultures grew more rapidly, but otherwise did not differ from the äerobic ones. They showed nothing to the naked eye until after five days, when they appeared as small, isolated, dewdrop-like particles, which did not become confluent. After eight days they increased in size, being about as big as

[1] *Bericht ueber die Sitzungen des* 3 *Medicin. Congresses, Russlands.* Wratsch, 1889, No. 2, p. 47; and *Centralbl. für Bacteriologie*, etc., 1889, Bd. v. s. 683.

[2] "Ein Beiträg zur Kenntniss dei Actinomykose," *Zeitsch f. Heilk.* August 1890, Heft iv. Bd. xi. s. 255.

[3] *Virchow's Archiv*, 1891, Bd. cxxvi.

a pin-head. Later they continued to grow, but very slowly, rarely getting any larger than a lint seed. At the same time they became whitish and more dense in the centre, which showed a prominent cone-shaped projection above the surface of the agar and rootlike processes, dipping down into the agar from the under surface. From the prominent centre, raylike projections passed outwards to the periphery of the nodule, thus giving it a resemblance to a rosette. The contour was nodular or smooth. They rarely became confluent or increased much in size, even after six months, although the larger ones frequently assumed a light yellow colour. They carried the cultures from the first case through fifteen generations, and from the second through twenty. When examined microscopically they found that after twenty-four hours only short bacillary forms, often thickened at one end, were seen. Much the same appearances were given for the next few days, the bacilli differing more in length, some remaining short, others becoming larger. After about seven days, short threads appeared, later cocci, and long dichotomously-branching threads. No clubs were seen. They inoculated rabbits and guinea-pigs successfully, but a sheep unsuccessfully, with their cultures, producing a typical actinomycosis, in which clubs were abundantly seen. From their observations they conclude—(1) the cocci do not multiply by division; (2) there is not yet sufficient evidence for regarding them as spores; (3) their significance is still undetermined, as there are objections to regarding them as a mere stage of growth, or as broken-down pieces of protoplasm; (4) the short bacilli form the filaments; (5) the clubs are involution forms. The evidence brought forward by all these culture investigations, however much they may differ in detail, is all in favour of the bacterial position of the actinomyces. I have already considered the question from its morphological side, and discussed the inter-relationship of the different elements. It will be remembered that, while the clubs were occasionally seen to be intimately connected with the ends of the filaments, there was no evidence to show that they were connected in any way with the processes of reproduction. I may here mention that apparent tranverse abscission of the ends of the clubs was occasionally seen in my sections, without, however, any

appearance of contained elements. This has often been observed, and I could see no reason for agreeing with Delépine that it was the result of mechanical pressure upon the cover glass. Sometimes definite cocci or bacillary segments have been seen within these separated portions of clubs, but no evidence has ever been advanced to show what the further changes are which occur in these bodies, without which the opinion that they act as organs of fructification must be regarded as a mere conjecture. An ingenious suggestion has been advanced by Delépine, viz., that the clubs are asci. He bases his suggestion mainly upon the remarkably analogy of arrangement there is between the parts of an actinomyces and those of the sphacelium of claviceps, one of the ascomycetes. While admitting the analogy, I have not been able to trace in the filamentous prolongations into the clubs any real resemblance to the processes characteristic of the formation of ascospores, with which I am fairly familiar. At the same time, I wish to state that my sections did not show any axial cavity such as he observed, and figures so clearly, and they do not support his contention so well as his own case. Mr. M'Fadyean [1] in an important and interesting paper on a case of "Bovine Actinomycosis," has added yet another link in the strong chain of evidence condemnatory of the importance of the clubs. He found that some of the *youngest* colonies are *entirely* composed of *cocci*, that many show a great preponderance of them, and that none, even of the smallest colonies, were entirely free from them. He further found reason for believing that the cocci multiply by division, and that some of them elongate into short bacillary forms, and through these to long filaments. It is obvious, then, that until some direct evidence of an actual participation of the clubs in the reproductive process is brought forward, we must regard the actinomyces as a pleomorphous form of the cladothrix group of bacteria, and not as a true fungus, a conclusion which Boström insisted on as early as 1885. He believed—and many observers have corroborated his view—that it closely simulates the *Streptothrix Försteri* of Cohn.

Etiology—1 *Geographical distribution.*—The patient was

[1] *Journ. Comp. Path. and Therap.* 1889, Part 1. vol. ii.

a Scotsman, residing in Kirkcudbrightshire, and his is the second case of actinomycosis described as occurring in Scotland, having followed upon the first[1] in little over sixteen months. It is rare in England, America, and France, while it is almost common in certain parts of Germany, Austria, and Russia. It would appear to be somewhat on the increase. The first case occurring in man was described by Israel[2] in 1879, but there is good reason for believing that Langenbeck had observed a case as early as 1845, and that Lebert[3] had, in 1857, seen and figured actinomyces colonies in pus taken from the human subject, though the organism being then unknown these observers failed to identify them. At the end of 1881 Ponfick[4] recorded 6 cases. In 1886, Moosbruger[5] published 75 cases collected from different sources, and towards the end of the same year other 14 cases could be added to his list. It was during this year that the first case occurring in England was described by Acland.[6] Over 300 had been observed up to the end of 1890, while to the same period of 1892 the number had increased to nearly 450. These are somewhat striking figures, and go far to show that the disease has become more common of late years. It is useless to urge that it has really largely escaped notice owing to the necessity of using special methods for its detection. These are not necessary, for it is easily recognised by the ordinary microscopical methods which have been in vogue for the last ten years; and while probably enough some cases may have been passed over, I think we must agree with Delépine[7] in believing their number to be small.

2 *Sex and age.*—The patient was a man 23 years of age. In looking over the records of the various published cases I made a note of the sex, age, and primary seat of the disease where possible, and have arranged the results in the following tables:—

[1] Vol. 1 of these *Reports*.
[2] *Virchow's Archiv*, Bd. lxxiv. s. 15, *et seq.*
[3] *Firket Revue de medicine*, 1884, p. 276.
[4] *Loc. cit.* 1882.
[5] *Ueber Actinomykose des Menschen.* Tübingen, 1886.
[6] *Brit. Med. Journ.* 1886, vol i. p. 1159; and *Trans. Path Soc. Lond.* 1886.
[7] *Loc. cit.*

HEAD AND NECK.

Age.	Males.	Total.	Females.	Total.	Sex not stated.	Total.	Total of both.
From 1– 5	2 at 5,	2	...	...	1 at 1, 1 at 4,	2	4
,, 5–10	...	...	1 at 8, 1 at 9, 1 at 10,	3	1 at 9,	1	4
,, 10–15	1 at 11, 1 at 12, 3 at 13, 3 at 14,	8	...	...	...	...	8
,, 15–20	1 at 16, 3 at 17, 2 at 18, 3 at 19, 10 at 20,	19	3 at 18, 5 at 19, 3 at 20,	11	1 at 17,	1	31
,, 20–25	8 at 21, 7 at 22, 7 at 23, 10 at 24, 3 at 25,	35	1 at 21, 2 at 22, 2 at 23, 3 at 24, 1 at 25,	9	1 at 24,	1	45
,, 25–30	4 at 26, 5 at 27, 4 at 28, 4 at 29, 3 at 30,	20	2 at 26, 1 at 27, 3 at 28, 2 at 29, 1 at 30,	9	2 at 27, 1 at 30,	3	32
,, 30–35	3 at 31, 2 at 32, 2 at 33, 1 at 34,	8	1 at 31, 1 at 34, 1 at 35,	3	1 at 31,	1	12
,, 35–40	5 at 36, 3 at 37, 8 at 38, 2 at 39, 2 at 40,	20	1 at 36, 1 at 37, 2 at 38, 2 at 40,	6	2 at 37,	2	28
,, 40–45	1 at 41, 2 at 42, 2 at 43, 3 at 44, 2 at 45,	10	1 at 42, 1 at 45,	2	..	...	12
,, 45–50	2 at 46, 1 at 48, 2 at 49,	5	1 at 46, 1 at 49, 1 at 50,	3	...	...	8
,, 50–55	2 at 51, 5 at 52, 1 at 53, 1 at 54,	9	1 at 51, 1 at 52, 2 at 54,	4	1 at 53,	1	14
,, 55–60	1 at 56, 3 at 57, 1 at 58, 1 at 59,	6	...	...	...	...	6
,, 60–65	1 at 62,	1	1 at 61, 1 at 62,	2	...	...	3
Over 65	...	...	...	...	...	...	...
		143		52		12	207

TONGUE.

From 20–25	1 at 24,	1	1 at 22,	1	...	...	2
,, 25–30	1 at 29, 1 at 30,	2	...	...	...	...	2
,, 30–35	1 at 35,	1	...	...	...	...	1
,, 35–40	1 at 36,	1	...	...	...	...	1
,, 45–50	1 at 48, 2 at 50,	3	...	...	...	...	3
,, 50–55	1 at 54,	1	...	...	...	...	1
,, 55–60	1 at 56,	1	1 at 56,	1	..	...	2
Over 65	1 at 74,	1	...	...	...	...	1
		11		2		...	13

Age.	Males.	Total.	Females.	Total.	Sex not stated.	Total.	Total of both.
From 5–10	1 at 9,	1	1 at 6,	1	...	...	2
,, 10–15	1 at 11,	1	1 at 13, 1 at 15,	2	...	...	3
,, 15–20	1 at 17, 1 at 20,	2	1 at 18, 1 at 19,	2	...	...	4
,, 20–25	2 at 21, 1 at 22, 1 at 25,	4	1 at 22, 1 at 24,	2	...	...	6
,, 25–30	3 at 26, 1 at 28, 1 at 30,	5	1 at 30,	1	...	...	6
,, 30–35	1 at 34, 1 at 35,	2	1 at 31, 1 at 33, 2 at 35,	4	...	...	6
,, 35–40	1 at 37, 2 at 39,	3	1 at 38, 1 at 39, 3 at 40,	5	...	...	8
,, 40–45	1 at 44, 1 at 45,	2	...	...	2 between 40 & 50	2	4
,, 45–50	2 at 46, 2 at 48, 1 at 50,	5	...	...	...	...	5
,, 50–55	1 at 51, 1 at 52, 1 at 54,	3	1 at 51,	1	...	...	4
,, 55–60	1 at 56, 1 at 60,	2	...	...	...	...	2
,, 60–65	1 at 63,	1	...	...	...	...	1
Over 65	1 at 67,	1	...	...	...	...	1
		32		18		2	52

ABDOMINAL.

From 10–15	1 at 15,	1	1 at 14,	1	...	...	2
,, 15–20	2 at 18, 4 at 19, 3 at 20,	9	1 at 16,	1	...	...	10
,, 20–25	1 at 22, 3 at 23, 2 at 24,	6	1 at 22, 1 at 24, 1 at 25,	3	...	...	9
,, 25–30	2 at 26, 3 at 28, 2 at 29, 2 at 30,	9	1 at 27, 2 at 28, 1 at 29, 1 at 30,	5	...	...	14
,, 30–35	2 at 32, 2 at 33, 2 at 34, 2 at 35,	8	2 at 32, 2 at 35,	4	...	...	12
,, 35–40	2 at 37, 1 at 38, 2 at 39, 3 at 40,	8	2 at 36, 1 at 37, 1 at 39, 1 at 40,	5	1 at 40,	1	14
,, 40–45	1 at 42, 1 at 43, 5 at 45,	7	2 at 45,	2	...	...	8
,, 45–50	3 at 46, 1 at 47, 1 at 48, 1 at 50,	6	2 at 50,	2	...	...	8
,, 50–55	3 at 51, 2 at 52,	5	...	...	...	...	5
,, 55–60	1 at 56, 1 at 60,	2	2 at 60,	2	...	...	4
,, 60–65	...	...	1 at 61,	1	...	...	1
		61		26		1	88

SKIN.

Age.	Males.	Total.	Females.	Total.	Sex not stated.	Total.	Total of both.
From 10–25	1 at 14,	1	...	...	...	...	1
,, 25–30	1 at 29,	1	1 at 28,	1	...	...	2
,, 30–35	1 at 34, 1 at 35,	2	...	...	...	...	2
,, 35–40	1 at 37,	1	...	...	...	...	1
,, 40–45	1 at 45,	1	...	...	...	...	1
,, 45–50	1 at 50,	1	...	...	...	...	1
,, 55–60	1 at 60,	1	...	...	...	...	1
Over 65	1 at 66,	1	...	...	...	...	1
		9		1		...	10

DOUBTFUL.

From 5–10	1 at 9,	1	...	...	...	...	1
,, 10–15	1 at 13,	1	1 at 14, 1 at 15,	2	...	...	3
,, 15–20	1 at 16, 1 at 17, 1 at 18,	3	1 at 20,	1	...	...	4
,, 20–25	1 at 22,	1	...	...	...	...	1
,, 25–30	1 at 27, 1 at 30,	2	2 at 26, 1 at 30,	3	...	...	5
,, 40–45	1 at 41,	1	2 at 44,	2	...	...	3
,, 45–50	1 at 50,	1	...	...	...	...	1
,, 55–60	1 at 56, 1 at 57, 1 at 60,	3	...	...	...	...	3
65 and over	1 at 65, 1 at 77,	2	...	...	...	...	2
		15		8		...	23

The total under each table shows that the disease is much more common in men than women in all its forms. In addition to these 378 cases, in which both sex and age are stated, I have found other 27 in which the sex alone is stated. This gives a total of 405 in which the sex is known. Of these 295 are males and 110 females, or a proportion of very nearly $2\frac{2}{3}$ to 1. Practically, then, we may say that the disease is very nearly three times commoner in men than women. Again, in its relation to age, it will be noticed that while it has been observed as early as 1, 4 and 5 years of age respectively, and as late as 77, it is not common before 10 or after 60; and while it is frequently met with at all intervening ages, the period of young adult life is apparently most favourable, more especially the third decade. The following list of 392 cases, in which I found a record of the age, shows very well its relative frequency during the different lustra:—

Age . . .	1–5	5–10	10–15	15–20	20–25	25–30	30–35
No. . . .	4	7	17	49	63	60	34
Age . . .	35–40	40–45	45–40	50–55	55–60	60–65	Over 65
No. . . .	52	28	26	24	18	5	5

Trade or occupation.—The patient was a baker, but almost every occupation or calling in life supplies instances, *e.g.* peasants, labourers, soldiers, watchmen, tailors, shoemakers, chimney-sweepers, waiters, gardeners, farmers, clerks, preachers, teachers, students, and doctors. Out of 100 cases taken at random, 10 were coachmen or grooms, 32 peasants or workers in the fields (5 of whom are specially mentioned as being much engaged about cattle), 25 were farmers, grieves, or landowners, 8 bakers or millers, 17 merchants or commercial travellers, 5 students, and 3 physicians. It attacks people in every rank of life, from noblemen to peasants, from ladies of rank and position to their humblest domestics.

4. *Contagion from cattle.*—The fact that the disease is

prevalent among cattle suggests the possibility of its direct transmission from them to man, but a consideration of the occupations of the patients shows that, while it is perhaps more commonly met with among those whose occupation is of the nature of an outdoor life, or such as might bring them in contact with cattle, its distribution is much too widely spread, and the evidence is too slight to support in the slightest degree the theory of transmission from contact with diseased animals. Indeed, veterinary literature contains no clear instance of its transmission, even from cow to cow, although Crookshank [1] records a case in which he succeeded in transplanting it from man to a calf.

5. *From flesh of cattle.*—I have carefully searched the literature of actinomycosis for reliable evidence, to show that there is danger in consuming the flesh of animals which had suffered from the disease, and I have found none. The great balance of opinion of veterinary experts leans to the view that there is practically no danger from this source, although a good many prefer to regard the question as still *sub judice.* It is interesting to note that Dr. D. E. Salmon of Washington stated in the discussion upon Dr. Crookshank's paper above referred to, that the utilisation of carcases of animals affected even in the slightest degree with actinomycosis is not tolerated in the United States.

6. *From milk.*—Bollinger [2] claims that milk was the probable source of injection in his case of primary actinomycosis of the brain. His proof is however slight, and chiefly inferential. His patient did not partake of flesh meat of any kind, nor vegetables, nor any form of grain for the last year of her life, but had lived mainly upon unboiled milk. It is easy to understand how milk-injection might readily occur, especially if the process of milking were carried on in the byres, and the milk allowed to remain there for any time. The parasite has never been found in the milk, and, moreover, I have shown that the disease is rare in childhood, there being only 4 cases described as occurring during the first five years of life. This contrasts strikingly with tuber-

[1] *Trans. Seventh Internat. Cong. Hyg. and Demog. Ref.* p. 196.
[2] *Münch. med. Woch.* 1887, No. 41, p. 791.

culosis, which is so common in children of tender years, and in which milk infection is completely established. In nearly half of all tubercular animals, the milk proves to be infected; and Bollinger, Hirschberger, and others, have shown that the milk may contain tubercle bacilli, even if the udders themselves are not tubercular. Infection of actinomycosis by means of milk would thus appear to be very improbable, but it is to be remembered that few attempts have been made to find the organism in milk, and further that it cannot be said with certainty that we know its appearances in its earliest stages. I have been greatly interested in finding the disease in the mammary gland of the cow. My attention was drawn to the case by Professor Mettam,[1] through whose kindness I obtained part of the diseased gland. It had been sent to Principal Walley along with several other diseased udders, all believed to be tubercular. After embedding in paraffin and cutting, I stained the sections in several different ways. They show an undoubted actinomycosis of the typical bovine form, being identical with that seen in other sections I possess, taken from affected tongues. Clubs are beautifully seen, but filaments and cocci are mostly absent. The nodules are multilobulated, as are also many of the individual follicles of which they consist. They lie among the areas of the galactophorous ducts. I cannot detect any actual invasion of the wall of any of these milk tubes, as there is always a capsule, more or less distinct, to be made out around the follicles. Some of the tubes, however, showed marked signs of disease, their lining epithelial cells being greatly swollen, staining badly, and being without nuclei. There is also in places a considerable amount of interstitial round-celled infiltration. It is thus seen that, although the actinomyces does not itself apparently directly invade the gland tubes in this case, it produces a considerable change in them of a hurtful character, and further that it is difficult to believe that the parasite does not in some form or other invade the tubes, as the two lie so close together, and are so intermingled. If so, its appearance in the milk is rendered very

[1] *Journ. Comp. Path. and Therap.* Sept. 1892, p. 245, footnote.

probable. I have not been able to discover any record in veterinary literature of the udder of cows being affected. John [1] and Ponfick [2] have described it in pigs, and accounted for it by the actinomyces gaining entrance by the teat-ducts; but, so far as I know, no instance in cows has hitherto been published. This case was discovered by chance, and it is difficult to believe that it is an isolated one. I have endeavoured to find and secure other examples, but have not yet succeeded. The contention, then, that milk may be a possible source of infection deserves some consideration.

7. *From certain cereals.*—There are good grounds for believing that the main cause of the disease is one common to both man and oxen. Among the lower animals it is confined to the ungulates, occurring in oxen, horses, and pigs, but there is one exceptional case in a carnivore, recorded by Vachetta,[3] as occurring in the jaw of a dog. It was long ago considered likely that the infection was brought about in some way by the food, and certain grasses, vegetables, and drinking waters have all in turn been regarded with suspicion, but the remarkable observations of Jensen [4] in 1880 focussed attention chiefly upon barley and kindred cereals. He observed that the disease was each year more or less prevalent in cattle, which had for several years been fed on barley grown on land reclaimed from the sea, and that on the late autumn of 1879, and the winter following, the outbreak was so great that nearly the whole herd was affected. In 1881 John [5] demonstrated actinomyces in vegetable substance in the tonsils of pigs, and in 1885 Boström [6] and Piana [7] independently observed and recorded the same phenomenon in the growths in the tongue of the ox in this disease. In 1888 Brazzola,[8] and in 1889 Hofmann,[9] made similar observations, the latter being in a

[1] *Centralbl. f. d. med. Wissen.* 1881.
[2] *Die actinomykose des Menschen*, 1882.
[3] *Clinica Veterinaria*, 1882.
[4] *Tidkrift f. Veterinær.* 1883.
[5] *Centralbl. f. d. med. Wissen.* 1881, p. 15.
[6] *Loc. cit.* p. 216, etc.
[7] *Archivio per le scienze mediche*, vol. x. p. 137. Torino, 1886. And *Rendiconto dell' Istituto anatomo-patologico della v. sucola, sup di medicina veter. di milano*, 1886, p. 1.
[8] *L'Ercolani*, Jan. 1888.
[9] *Zur Casuistik der vom Pharynx ausgehenden aktinomykose.* Giessen, 1889.

case of the disease in the pharynx of a man. In 1885 Soltmann[1] recorded a case of mediastinal actinomycosis in a boy, in which he believed the infection to be due to the perforation of the pharynx by an ear of barley accidentally swallowed by him. Other observers have also made observations supporting the view of infection by the grains of certain cereals, but the most remarkable evidence is that led by Boström, who, in 11 cases of the disease in the human subject, found in the local lesion remains of grains of barley or corn, or other cereal, with the actinomyces growing abundantly in and from them. The enormous labour and care involved in these investigations cannot be overrated, involving as they did the examination of thousands upon thousands of sections. In the case before us I was unable, either macroscopically or microscopically, to find evidence of the presence of any cereal grains in whole or in fragments, although I examined an immense number of sections; but on inquiry I learned from the friends of the patient that he was constantly, in his employment, being baker to a large firm of general grocers, brought in contact with all sorts of dry grain, and moreover was in the habit of carrying these, along with peas, etc., in his pockets, and was frequently seen to chew them. This habit of frequently chewing grain, peas, sweets, etc., was so noticeable as to be commented upon by his friends and employers. His friends assert that his appetite was large until the end of 1892, and even later; that he often brought home heads of corn and other grain on returning from a walk through the fields; and that he was often seen to place the grain in his mouth. His companions used to chaff him for eating such things. Oats are chiefly grown in the part of the country in which the patient resided, but barley and wheat also to some extent.

In the absence of any trace of grain fragments in the local lesion, this evidence can only be accepted as probably pointing to the manner of infection; but it is to be remembered that the parts were not entirely undisturbed, as some displacement may have taken place during the operation, and further that I have brought forward reason for believing that discharges into the intestine will frequently take place,

[1] *Jahrb. für kinderh.* N. F. xxiv. s. 129.

and it is possible therefore that the grain fragment or fragments may at some time or other have been in this way discharged along with the excreta.

8. *Mode of entrance of the parasite into the body.*—As will be observed from the tables given above, the primary lesion may be either in the head or neck, the tongue, the lung, or thorax, the intestines or abdominal cavity, or in the skin. There are, in addition, cases in which it is difficult to determine the primary seat. Some of these, I think, might with propriety be placed under the headings of abdomen or skin, but in the absence of certain proof, perhaps, it is better to place them tentatively. Israel [1] makes three classes—(1) the jaws, (2) the lungs, (3) the intestines, and adds a fourth in which the mode of entrance is unknown. Rütimeyer [2] gives the percentage as follows—50 per cent. in head and neck, 25 per cent. in lungs, 15 per cent. in intestines, and the remaining 15 per cent. indeterminate; but out of a total of 430 cases of which I have found sufficient records, the proportion is rather different, viz., 224 being in the head and neck, 16 in the tongue, 57 in the lungs, 93 in the abdomen, 11 in the skin, and 29 indeterminate; giving a percentage as follows. Taking in the tongue cases, along with those of the head and neck, $55\frac{3}{4}$ per cent. in head and neck, $13\frac{1}{4}$ per cent. in lungs, $21\frac{3}{5}$ per cent. in abdomen, $2\frac{1}{2}$ per cent. in skin, and $6\frac{9}{10}$ per cent. indeterminate. The largeness of the proportion in the head and neck is no doubt to be accounted for by infection through the mouth. In the process of chewing the grain husks, etc., minute wounds might arise in the mucous membrane of the jaws, cheek, or tongue, through which the actinomyces might effect an entrance; or the grain débris containing the parasite might collect around and find an entrance through a carious tooth, as Israel [3] pointed out; and this may be an explanation of the more frequent occurrence of the disease near the lower than the upper jaw, and near the back part rather than the front part of the mouth. Some believe that the parasite may enter by

[1] *Actinomycosis in Man*, Sydenham Society, 1886.

[2] "Ein Fall von primärer Lungenactinomycose," *Berlin. klin. Woch.* Nos. 3 and 4, 1889.

[3] *Loc cit.*

Stenson's duct. The infection may, however, take place lower down, as instanced by Soltmann's case, in which the pharynx, by Boström's, in which the œsophagus, were respectively perforated by the grain spikelet; or it may pass further down and effect a lodgment in the stomach, duodenum, large intestine, or vermiform appendix. Samter thinks that it may be retained in the intestine for some time, wandering up and down it. Primary infection of the lungs can only be explained by inhalation; of the skin, by constant rubbing or friction, as instanced by the cases occurring on the hands of peasants engaged in hoeing or mowing, and of persons addicted to the apparently innocent game of skittles. This last method of infection is comparable to that which takes place in animals, which probably become infected by rubbing themselves against fences, trees, walls, straw, etc. It may spread from the skin to the lungs. Cases have been recorded by Samter and others, in which actinomycosis occurred at the seat of a severe bruise upon the thorax, and gradually extended through to the pleura and lungs. It may also invade the lungs from the œsophagus, or vertebral column or liver. Secondary intestinal infection may occur in cases of primary pulmonary disease from swallowing the sputum, as in phthisis. This would seem to show that the parasite can enter the intestinal tract otherwise than when protected from the gastric juices by the grain coats. We do not yet know what form it then takes, or how it escapes destruction in the stomach, for we know that the mature parasite is easily killed by dilute acids and various disinfectants. Intestinal lesions are more frequent in the small than in the large intestine, which is, in itself, in favour of the infection existing in some very minute form. Peristalsis is so much more active in the upper than in the lower gut that its contents are more rapidly hurried onwards; but we can easily understand how some minute form, such as cocci or bacilli, might find a lodgment in the mouths of Lieberkühn's follicles, and thus form the primary seat of disease. In the present case, whatever may have been the method of infection, its primary seat was in the hepatic flexure of the colon, and thence it spread by direct contact to the tissues around,

notably to the liver. It is much more difficult to explain its spread to the lungs. It will be remembered that the actinomycees colonies were seen in the bronchi, bronchioles, and a few air vesicles, pointing to inhalation as the method of infection. In the cases of Taylor and others, there were miliary tubercles found in the lungs, and the manner of spread was fairly clearly by means of the blood vessels or lymphatics. This method of extension is rendered highly probable by the observations of M'Fadyean, Delépine, and others, who observed cocci and bits of filaments within the protoplasm of leucocytes. I have also in my specimens found examples of leucocytes, which had ingested cocci, short bacillary forms, and threads. In no place did I observe actual invasion of the blood vessels, unless the plugs of micrococci mentioned as being present in a few of the blood vessels of the liver, spleen, kidneys, etc., are to be regarded in this light. It is also noteworthy that in no part did I find any evidence to support the spread of the disease by means of the lymphatics. All the lymphatic glands I examined were either healthy, or the seat of simple abscesses. If the lung affection arose through an extension of the disease, by means of the blood vessels, its distribution in the lung tissue is certainly most peculiar and difficult to explain. The infected leucocytes on leaving the blood vessel would have to pass through the alveolar wall to gain the alveolar passage, and thence the bronchioles. It is difficult to understand how this could take place, without, as in tubercle and other cases just referred to, reacting upon the endothelial cells, and setting up more considerable catarrhal changes that are here observed. The other method of infection, viz., through the air-passages, by inhalation, would certainly seem to be the more probable. The supposition that the lung infection was primary, and that of the intestine secondary, is impossible alike on pathological and clinical grounds. The pathological changes indicate that the intestinal lesions were probably of some months' duration, and the pulmonary only of a few weeks, probably two or three. The alveolar catarrhal changes and localised intestinal increase of tissue were of older date, but there was nothing indicative of

an actinomycotic nature in them, and it is to be remembered that he worked in an atmosphere more or less impregnated with flour and other dust particles. Clinically, the earliest evidence we have of any respiratory trouble is in May, when he had a cough and a nasal discharge. This seems to have quickly subsided, and was probably a simple cold. In June his lungs were examined, and nothing abnormal was detected, His cough and expectoration is said to have returned towards the end of August, but seem to have made more impression upon his friends than upon himself, and when he was admitted to the Royal Infirmary he had almost none. Physical examination of his chest revealed nothing, the breath sounds being normal and accompaniments absent. His sputum was examined by the Ziehl-Neelsen method, and gave negative results. No change was observed in his lung condition, until about the beginning of October, a few days after the operation. He then seemed to develop pulmonary symptoms somewhat suddenly, his cough becoming troublesome, and the sputum increasing in quantity. This condition became more and more pronounced, and although no dulness or other signs of consolidation were observed, plentiful accompaniments to the respiratory sounds appeared. No further examination was however made of his sputum, as attention was chiefly directed to his abdominal condition. Had the former examination been repeated, there is little doubt that the actinomyces would have been discovered, a supposition which is fully justified by its presence within the bronchial pus. This is further interesting, as it serves to show that the sputum may, in a very early stage of pulmonary actinomycosis, give clear evidence of the nature of the disease. It is extremely rarely that it is limited to the bronchi; indeed, the evidence that it may be so would seem to depend entirely upon Canali's[1] remarkable clinical case of a girl 15 years old, who apparently suffered from a chronic bronchitis only, and in whose fœtid sputum—which separated on standing into two, not three layers, as in the putrid sputum of many cases of bronchiectasis—the actinomyces was abundantly present. The condition has never been verified by post-mortem. Inasmuch

[1] "La broncoactinomycosi nell' uomo," *Rivista clinica*. Bologna, 1882.

as, however, the commoner lesions of pulmonary actinomycosis viz., broncho-pneumonia, abscesses, interstitial, and other consolidations, pleurisy, and empyema, may in many cases begin as a bronchitis, it appears likely, as seen by the present case, that the actinomyces ought to be found in the sputum at a very early stage. There are a goodly number of cases of pulmonary actinomycosis on record, in which the disease was diagnosed from the sputum during life, *e.g.* those of Israel, Braun, Affanassieu, Canali, Eichwald, etc., but we somewhat lack information as to what period of the disease we may reasonably expect to do so. It is in this view that I think the early appearance in this case to be of much interest. It would here appear that the pulmonary infection had taken place after his entrance into the Infirmary, or very shortly before it, as it is hardly likely that the organism would remain dormant in the passages for any length of time after its inhalation. Now as the intestinal infection must have occurred months before, this necessitates either a fresh infection altogether, or a lingering of the first infection in his mouth, perhaps about his teeth, for a very long period. His teeth were examined at the time of the sectio, and noticed to be in fairly good condition. One of the front upper incisors was broken and decayed, and two or three of the molars had discoloured tartar around their roots, but scrapings from these yielded negative results. This solution is one which it is most difficult to accept, and yet it is most in accordance with both the clinical and pathological data.

Treatment.—I am led to speak shortly on this question from certain appearances presented by the colonies under microscopic examination. There are abundant evidences of both degenerative changes and retarded growth in immense numbers of the colonies, indeed in all parts of the growth which lay nearest to the colon. I feel inclined to attribute this largely to the iodoform which was plentifully present around the colon for the last three weeks of the patient's life. There are many instances in the cases of Boström, Illich, Samter, and others, which amply support the value of iodoform in treatment. Complete excision is, where possible, of course to be recommended, but there are many cases of jaw and neck actinomycosis in which recovery followed upon the

use of corrosive-sublimate lotions and iodoform, applied to and around the lesion. About six or seven years ago, Thomassen of Utrecht recorded the value of the internal administration of iodide of potassium, combined with the local application of the tincture of iodine, to the affected tongue in bovine actinomycosis. He subsequently gave up the tincture and used the iodide alone in large doses, and with remarkable success. His treatment did not seem to have been generally known or adopted until about a year ago. He had then treated successfully over 80 cases, and asserted that the treatment never failed. More recently, Nocard [1] of Alfort reported 3 cases of bovine actinomycosis of the jaws to have been cured by Thomassen's iodide treatment. Since then several other successful cases have been noted both here and in America, *e.g.* by Gibbings,[2] Reeks,[3] M'Fadyean,[4] and others. The iodide was given in large doses—2 to 3 drachms daily. So far I have referred only to bovine actinomycosis, but Thomassen, in Nocard's [5] paper just mentioned, gives an account of the successful treatment of human cases by the same means. His first case, a captain in the navy, had suffered for months from actinomycosis of the floor of the mouth, with perforation in the submaxillary region. Iodide of potassium was given in doses of 20 to 30 grains daily, with the result that the patient immediately and steadily improved until recovery was complete, only a cicatrix remaining to mark the site of sinus. In the second, the patient, a tailor, was, on the 10th April 1892, operated on for what was thought to be a simple perityphlitis. Pus escaped, and the wound was dressed with iodoform gauze. Patient left Hospital apparently cured on 30th April. He was readmitted on 28th May, as the wound had reopened. Actinomyces bodies were now observed in the pus. Iodide of potassium was given on 4th June, in 15-grain doses daily, until the 15th June, when 20 grains were given. He left the Hospital apparently cured on the 30th of June, and when examined on the 14th November there was no sign of the disease returning. In the third, the patient, a

[1] "Rec de Medic. Veterin." 1893. Ref. *Journ. Comp. Path. and Therap.* June 1893.

[2] *Journ. Comp. Path. and Therap.* Dec. 1892.

[3] *Ibid.* June 1893. [4] *Ibid.* June 1893. [5] *Loc. cit.*

woman aged 49, had been ill for seven or eight months, and had developed a painful swelling in the right temporal region, which, on being cut into, exuded some pus in which the actinomyces was detected. Iodide of potassium, in doses of 30 to 40 grains, was given daily, along with gargles of permanganate of potash. In a little over a month the cure was apparently complete. The fourth, a farmer æt. 38, who suffered from an extensive and long-standing actinomycosis of the left side of the neck, after vigorous surgical treatment had failed, began speedily to improve upon 30-grain doses daily of the iodide, and in about seven weeks after (15th January 1893) was practically cured. There are other successful cases besides these of Thomassen's, *e.g.* those of Buzzi and Galli-Valerio in 1892, and Netter in 1893, to which I had referred in this paper, which was written before Ransom's interesting communication appeared in the *British Medical Journal*, January 13, 1894. I now consider it unnecessary to give any details regarding them as they are referred to in his paper. He records a successful result in his own case of the disease in the prostate and rectum, chiefly he believes, under the iodide of potassium treatment. There has been no return of the disease since November 1891. He has sufficiently emphasised the importance of the iodides, which would so far appear to be as great a specific in actinomycosis as they are in syphilis. Against these favourable results we have to note that several of the cases occurring before Thomassen's method was known, *e.g.* Eve's, were treated locally with iodoform and internally with both corrosive sublimate and iodide of potash, without any apparent benefit. Large doses of the iodides would seem to be necessary, and there is at least sufficient evidence in favour of their efficacy to warrant their careful trial in all cases. Mention might be also just made of Ziegler's[1] case of severe actinomycosis of the head and neck, in which he injected (25 injections in all) bacterial protein obtained from *Staphylococcus aureus*, with a favourable result; and of Billroth's[2] case which improved under tubercular injections.

[1] *Münch. med. Woch.* 1892, Bd. xxxix., s. 406.
[2] *Wiener. med. Woch.* 1891, No. 10, s. 142.

DESCRIPTION OF PLATES.

PLATE I.

FIG. 4.—Section of the liver, showing invasion by the actinomycotic growth. The liver cells are shown surrounded by a fine intercellular and pericellular fibrous tissue. The portal tracks are cirrhosed, and are still prominently seen, although the actinomycotic growth has advanced beyond them into the liver substance. This growth is of considerable thickness in this part of the section, and the clear space indicates that part of it has been omitted in order to show more of its characteristic features. In the upper part it shows the typical fine reticulated fibrous tissue, invaded at its lower part by large abscess cavities. Actinomyces colonies of different ages and growth forms are shown partly lying in the fibrous tissue and partly in the pus. All the colonies are faithfully represented, but two of them for convenience of illustration were transferred from another microscopic field to this. Stained with Gram and Biondi. × 50.

a. Atrophied liver cells showing intercellular cirrhosis.
b. Cirrhosed portal spaces showing portal vein, hepatic artery, and bile-ducts.
c. Fine reticulated fibrous tissue of the new growth.
d. Young blood vessel. Many of the vessels are so small as to be seen with difficulty by this power, and their walls are more delicate.
e. A young radiate colony lying in the fibrous tissue. Another, somewhat similar but more loosely arranged, is seen to the right. A small portion of a third colony is closely applied to the periphery of the latter.
f. An older more slowly-growing oblong colony lying free within the pus.
g. A cluster composed of an arc-shaped colony to the right, a young radiate colony below, and a few loose filaments belonging perhaps to a third colony to the left. A giant cell, with some connective tissue, and pus cells, are seen immediately above the cluster. It probably represents a follicle with extension of abscess formation into it.
h. A loose reticulated colony lying close to the wall of an abscess.
j. A young hollow sphere colony lying free in the pus.
k. Abscess cavities.
l. A dense arc-shaped colony, tending to curve quickly.

PLATE II.

FIG. 5.—Transverse section of wall of colon at a short distance from the gangrenous area, showing abscess cavities in the submucous coat, in one of which actinomyces colonies are seen. This cavity is seen to be extending especially towards the lumen, as tiny blood vessels lie almost isolated within the pus. The fibrous walls of the abscesses show a delicately reticulated, richly vascular tissue. One of the abscesses lying immediately below the mucous membrane has ruptured the muscularis mucosæ, and almost reached the surface. Stained with Gram and Biondi. × 50.

a. The mucous membrane showing Lieberkühn's follicles, etc. The surface epithelium is shed.
b. The muscularis mucosæ ruptured at one point.
c. The greatly thickened submucous coat infiltrated with many abscesses with reticulated vascular fibrous walls.
d. The circular muscular coat, somewhat thinned opposite the thickest part of the abscess cavity lying internal to it. The internal margin shows a very slight infiltration with leucocytes.

e. Abscess cavity separated from lumen by a thin layer of fibrous tissue infiltrated with leucocytes. The surface epithelium over it is shed. It is continuous through the muscularis mucosæ, with an abscess lying in the submucous coat.

f. New formed blood vessels, some considerably dilated, of the reticulated tissue, forming the partitions between the abscesses.

g. Lieberkühn's follicles, showing in places an increased fibrous tissue formation between them.

h. Actinomyces colonies lying free within the pus. A young radiate one is seen to the left, while in the large cluster two arc-shaped ones are seen above, two radiate ones, and a loosely arranged one below. Clubs appear on the part of the convex margin of the arc-shaped colony to the left.

PLATE III.

FIG. 6.—Transverse section of part of a bronchus, in a condition of subacute inflammation, showing a purulent plug occupying the somewhat dilated lumen. Two actinomyces colonies and many desquamated columnar epithelial cells are seen lying in the pus. The larger blood vessels are dilated, and many young vascular buds are seen passing inwards towards the lumen. Stained with Gram and Biondi. × 50.

a. Pus cells.

b. Ciliated columnar epithelial cells, desquamated.

c. A loose cluster of actinomyces, probably consisting of several colonies growing together. Clubs are seen at one part towards the left. The large colony towards the right is a beautiful example of the oblong growth form, showing little dense outgrowths from both sides of the main growth, and an extremely rich arrangement of long radiating mycelial threads all round, but more particularly to the left. It is a vigorous and actively-growing colony.

d. Circular muscular fibres.

e. Round cells close to inner margin of wall, forming a lining to the lumen.

f. Dilated blood vessels.

g. Pulmonary alveoli, very little altered.

h. Bars of hyaline cartilage.

i. Young vascular bud.

PLATE IV.

FIG. 7.—An irregularly-oblong colony of a looser arrangement than usual, showing a close network of filaments and marginal clubs. It lies in a small abscess cavity. Stained with Gram and Biondi. × 600.

a. The filaments.

b. The clubs.

c. Pus cells.

d. Connective-tissue cells.

FIG. 8.—A hollow sphere colony. The dense parts consist of a close network of filaments and short rods. Cocci are doubtfully present, and only in small numbers. Loose threads radiate outwards from the convexity, and are surrounded by a hyaline matrix. A shrub-like process is given off at one part of the convexity. The colony lies in a large abscess cavity. No clubs are present here, although plentifully seen in other similar colonies. Stained with Gram and Biondi. × 250.

a. The growing ends of the colony which have curved round and met one another.

b. The older part of the colony.

c. Outward prolongations of the growing ends, caused by a continuance of their growth after meeting one another. They may also be regarded as shrub-like processes.

d. A characteristic shrub-like outgrowth.

e. Imprisoned pus cells.

f. Pus cells surrounding the colony at a distance from it, except at one little cluster.

FIG. 9.—An actinomycotic follicle, showing the actinomyces in the centre, surrounded by epitheloid and round cells, with giant cells towards the periphery, where it passes insensibly into the fine reticulated fibrous tissue of the growth. Stained with Gram and Biondi. × 200.

a. The filaments of an oblong colony, with clubs towards the lower border. Portions of another colony or colonies are seen immediately above it.

b. Epitheloid cell.

c. Giant cell.

d. Capsule of fine fibrous tissue.

FIG. 10.—A giant cell, showing a homogeneous undegenerated protoplasm, containing nuclei and actinomyces, either a single-branched colony or separate closely-approximated colonies. Stained with Gram and Biondi. × 1000.

a. The clubs, mostly fine clavate forms, some being branched.

b. Filaments showing interrupted protoplasmic contents.

c. Nuclei of the giant cell.

PLATE .

FIG. 11.—Artificial culture of eight days' growth, showing small cocci and short rod-shaped forms. The former vary in size and the latter vary in length, while some of them are thicker at one extremity. They show a great tendency to arrange themselves end to end in lines, so as to give the appearance of filaments, which here and there seem to branch. This branching sometimes resembles a true dichotomy, at others an accidental arrangement of the elements so as to simulate this condition. Stained with methyl-violet. × 1200.

PLATE .

FIG. 12.—Artificial culture of twelve days' growth, showing a rich network of filaments with numerous cocci. Some of the filaments show a continuous protoplasm, sometimes with a club-shaped extremity, others a discontinuous or interrupted protoplasm, the individual elements varying much in length. Many of the filaments show a true dichotomy. The cocci vary much in size, some are small, others large, and there is every gradation between them and the short rods. Stained with methyl-violet. × 1200.

PLATE .

FIG. 13.—Artificial culture of fifteen days' growth, which so closely resembled that of a twenty days' growth as to make a separate drawing unnecessary. It shows branching delicate filaments, some of which are of great length. The cocci are not now so numerous. The tendency of the filaments to spiral, wavy, and twisted growths is well seen. Their protoplasm is nearly always interrupted, and the individual elements, cocci and rod-like, often lie at considerable distances apart. The ends are often clavate. Stained with methyl-violet. × 1200.